

Laboratory Medicine: A National Status Report

Prepared for:

Division of Laboratory Systems
National Center for Preparedness, Detection, and
Control of Infectious Diseases
Centers for Disease Control and Prevention

Prepared by:

The Lewin Group
Under subcontract to Battelle Memorial Institute

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Prepared by:

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EXECUTIVE SUMMARY

Although the U.S. ranks highest in per capita health care spending, there is overwhelming evidence of gaps between well-founded standards of care and health care practice. The Institute of Medicine reports, *To Err is Human: Building a Safer Health System* (1999) and *Crossing the Quality Chasm: A New Health System for the 21st Century* (2001), and other sentinel studies have focused national attention on improving the quality and safety of health care. Stakeholders agree that the quality of care delivered in the U.S. is inadequate and that the organization and delivery of health care must be improved.

Given the shortfalls in quality and continued escalation in costs, health care must be assessed continually to inform decision-making, and redesign delivery and incentives as needed, to yield appropriate, high quality care. An integral component of care is laboratory medicine, which extends across research; screening, diagnosis, and treatment; and public health. Appropriate use of laboratory testing is essential for achieving safe, effective, and efficient care to patients.

Health care must be informed by data derived from scientific assessment of efficacy and effectiveness of procedures, and must adapt to ongoing changes in science, technology, and practice.⁹ Laboratory medicine is not only responding to these changes, but is contributing to them in an environment of demographic, social, and economic change.

The Centers for Disease Control and Prevention (CDC) has commissioned this report to contribute to the groundwork for transforming laboratory medicine over the next decade. CDC charged The Lewin Group, under subcontract to Battelle Memorial Institute, with drafting this document, *Laboratory Medicine: A National Status Report*. The report examines in detail the key factors affecting the laboratory medicine sector, and is organized into chapters on the following main topics:

- Value of laboratory medicine
- Market profile of the laboratory medicine sector
- Laboratory medicine workforce
- Quality and the total testing process
- Quality systems and performance measurement
- Laboratory information systems
- Federal regulatory oversight of laboratory medicine
- Reimbursement for laboratory medicine

THE VALUE OF LABORATORY MEDICINE TO HEALTH CARE

Laboratory testing has a major effect on clinical decisions, providing physicians, nurses, and other health care providers with information that aids in the prevention, diagnosis, treatment, and management of disease. Despite this scope of influence, spending on laboratory services accounts for only 2.3% of U.S. health care expenditures and 2% of Medicare expenditures.

- Laboratory tests provide objective data about patient health that enable screening for risk factors, accurate and early diagnosis, determination of disease severity and likelihood of recovery, selection and monitoring of treatment, and evaluation of potential adverse outcomes. Some laboratory tests are vital to patient self management of chronic conditions.
- Information provided by laboratory testing is critical for maintaining quality and safety, including the prevention of adverse reactions. For managing medication, testing provides information for maintaining optimum drug levels, helps to detect and recover from medication errors, and enables use of genetic information to guide personalized prescribing. Laboratories protect the blood supply from pathogens and accurately match patients and blood products.
- Services provided by clinical laboratories are critical to public health at the individual and population levels by identifying nosocomial infections, antimicrobial resistance, infectious disease outbreaks, exposure to toxic substances, and chemical and biological threats. Laboratories also help to mitigate the effects of natural disasters by enabling rapid turnaround of tests used during triage and emergency care of individual patients as well as tests to confirm the presence of communicable diseases that threaten the population.
- Laboratory medicine supports the practice of evidence-based medicine and is being incorporated into clinical practice guidelines, which assist practitioners and patients in making decisions about individuals' health care in specific circumstances.
- Laboratory testing is one of several important indicators for assessing quality of care, particularly for national priority health conditions such as diabetes, heart failure, and colon cancer. Laboratory data can be used in support of value-based purchasing.
- Greater attention by providers and payers to evidence-based medicine, practice guidelines, and quality indicators is contributing to more appropriate use of laboratory tests, diminishing both overuse and underuse of tests.
- The evidence base for the cost-effectiveness of laboratory tests, and the broader therapeutic regimens and other interventions of which they are a part, is growing. This evidence is helping to inform appropriateness of test selection and sequencing, technology acquisition decisions, formulary design (including for pharmacogenomic-mediated therapies), and screening and other population-based interventions. It is also being considered in selected coverage and payment policies of some health plans and other third-party payers.

MARKET PROFILE OF THE LABORATORY MEDICINE SECTOR

The revenue, spending, and test volume of the U.S. clinical laboratory testing market has grown steadily over the past decade. Market expansion is attributed to changes in demographic factors and burden of disease; scientific, medical, and technological advances; and increased consumer awareness and self care.

- Based on 2007 data from the Centers for Medicare and Medicaid (CMS) Online Survey, Certification, and Reporting (OSCAR) database, CDC estimates that approximately 6.8 billion laboratory tests are performed annually in the U.S. Other data from 2007 evaluations indicate the following regarding the extent of the market for laboratory tests.
 - Laboratory testing revenues were a projected \$52 billion in 2007.
 - Clinical pathology comprises 66% of all laboratory tests and \$32 billion in revenue.
 - Anatomic pathology and cytology account for 23% of laboratory tests and \$11 billion in revenue.
 - Molecular and esoteric (e.g., low volume tests such as those for rare diseases) testing account for 8% of laboratory tests and \$4 billion in revenue.
 - Drugs of abuse testing accounts for 3% of laboratory tests and \$1.5 billion in revenue.
- More than 4,000 laboratory tests are available for clinical use. Of the 1,162 tests that are reimbursed by Medicare, about 500 are performed regularly.
- The number of genetic tests is growing. An estimated 1,430 diseases are now detectable using genetic testing; of these, an estimated 287 are tested only in research settings.
- The number of Clinical Laboratory Improvement Amendment (CLIA)-certified laboratories has grown to exceed 200,000 in 2007. Physician office laboratories represent 54% of clinical laboratories in this sector, four out of five of which are certified to perform only waived and/or provider-performed microscopy tests (e.g., rapid streptococcal detection, wet mount examination).
- Hospital-based laboratories account for the largest proportion of total testing volume (55%) and generate the highest proportion of total testing revenue (54%), projected at \$28.4 billion for 2007. From 1999 to 2006, the average annual growth rate of both test volume and revenue was approximately 6-7%. In 2006, privately-owned laboratories generated revenues of \$15.5 billion (32% of total laboratory testing revenue that year).
- Consumer directed testing is a key area for market growth. In 2004, 10-15% of hospital and commercial clinical laboratories offered some form of direct access testing. Laboratories should be prepared to assume a greater advisory role and provide other support to promote informed self care by consumers.
- Publicly available information about the economic status and quality of the laboratory medicine sector remains limited. The main current sources are CMS' OSCAR database, ad hoc surveys, and commercial market reports used for investment purposes. As a

group, these leave certain gaps in covering the laboratory market, including reliable estimates of market revenues, spending, test volume, and laboratory testing trends.

LABORATORY MEDICINE WORKFORCE

Comprising pathologists, doctoral-level laboratory scientists, technologists/scientists, and technicians, the laboratory medicine workforce has a vital role in the health care system, managing and applying evidence-based, scientific testing techniques to support patient care and protect against public health threats. However, there is growing concern regarding shortages in the number of laboratory professionals entering the workforce. The shortage could become pronounced with the forthcoming retirement of many laboratorians. At the same time, the demand for laboratory services continues to increase. Innovative technologies are changing the practice of laboratory medicine, educational requirements and staff qualifications.

- In 2005, there were an estimated 19,339 pathologists in the U.S., including 80% in community practice. Minorities are under-represented in the discipline of pathology, with 10% identified as Asian, 3% Hispanic, and 1% African American. Slightly more than half of pathology residents are female.
- An estimated 160,760 medical technologists/scientists (including cytotechnologists) and 144,710 technicians were employed in the U.S. in 2006. While nearly three-fourths of this workforce is female, it is more representative of the diverse ethnic makeup of the population, i.e., 12% Asian, 11% African American, and 7% Hispanic. By type of region, 58% of technologists/scientists work in an urban setting, 24% in suburban, and 18% in rural.
- The number of technologist/scientist and technician education programs has declined by more than 50% since 1970, with the most dramatic decline in technologist/scientist programs, 71% of which closed between 1970 and 2007. In contrast, the number of phlebotomy training programs increased six-fold from 1987 to 2003.
- Current enrollment in specialized technologist/scientist and technician educational programs is lowest in blood banking and histotechnology. Recent recruiting efforts appear to be effective, specifically those targeted at recruiting minorities and males.
- The shortage of technologists/scientists and technicians is expected to worsen over the next decade with demographic changes and retirements. Although personnel vacancies were highest in 2000 (11-22%), they remained steady from 2002 to 2005 at an annual rate of 4-7%. Vacancies vary according to staff position, laboratory type and size, and geographic location.
- Technological advances will change the qualifications required of the next generation of laboratory professionals. The laboratory sector needs to clearly redefine staffing qualifications and workforce level requirements accordingly.

QUALITY AND THE TOTAL TESTING PROCESS

The total testing process (TTP) defines the preanalytic, analytic, and postanalytic phases of laboratory testing, and serves as the basis for designing and implementing interventions, restrictions, or limits that can reduce or remove the likelihood of errors. Despite continued

improvements, many sources of error remain to be addressed. Higher rates of error occur in the preanalytic phase of testing, but the distribution of errors can vary widely among institutions, settings, and types of tests. Estimated error rates by phase of testing are in the ranges of 32-75% in the preanalytic phase, 13-32% in the analytic phase, and 9-31% in the postanalytic phase. Some errors that occur in the analytic phase originate with errors in preanalytic processes.

Chief issues affecting quality include poor communication and insufficient knowledge of tests that occur most often during test selection/ordering and interpretation of results. Common errors in clinical and anatomic pathology involve patient and/or specimen misidentification, specimen collection errors, and specimen contamination. Test turnaround time and notification of critical values are frequently cited for ratings of below-average to poor in customer satisfaction surveys. Medical and scientific advances, such as in genetic testing, will raise further quality challenges.

- Lack of uniformity and standardization of clinical pathology test values among manufacturers hinders implementation of laboratory-based guidelines, which require method-dependent decision limits. Heterogeneity of test values also makes it difficult for clinicians to work in an integrated health system using more than one testing method, or to address the needs of special patient populations.
- Laboratorian consultations are standard practice and reimbursed for anatomic pathology, but this is not always the case in clinical and molecular pathology. The primary barriers to interpretive consultations in clinical pathology reports are lack of reimbursement for such consultations and the shortage of subspecialty expertise. Expanded consultation services to clinicians would contribute to improved patient care and outcomes.
- Quality control (QC), performance evaluation, and test reproducibility standards to minimize diagnostic discrepancies and errors have been better defined and applied in clinical pathology than in anatomic pathology. Such measures should be developed for anatomic pathology.
- Standardization of data elements and report formats for all laboratory tests is necessary to improve physician comprehension and use of results as well as to integrate report data into clinical practice information technology applications. Better use of graphical displays in results reports is especially important for new proteomic and genetic tests.
- Effective technologies and strategies to reduce identification-related errors include use of barcoded labels for containers and slides, inpatient wristbands, and computerized physician/practitioner order entry (CPOE). Automated analyzers and results verification have decreased cognitive-related errors in clinical pathology, while external, secondary consultation in anatomic pathology can help decrease errors for complex cases.
- Point-of-care testing (POCT) has the potential to significantly enhance the quality of care, although additional research is needed to identify the best methods for integrating POCT into daily clinical processes and improving its accuracy as needed. Operators of POCT devices must be trained appropriately in testing practices.

QUALITY SYSTEMS AND PERFORMANCE MEASUREMENT

Achieving consistently high levels of quality in laboratory medicine calls for moving beyond stand-alone, analytic-focused, QC, quality assurance (QA), and proficiency testing (PT) activities. It requires more comprehensive quality management systems (QMS), such as those espoused in ISO 9001:2000 and ISO 15189:2003 standards. Performance measurement is an important component of QMS and has been a core feature of quality improvement programs across many industries. In laboratory medicine, the great bulk of effort on formal performance measurement and improvement to date has focused on the analytic phase, with insufficient attention to the pre- and postanalytic phases.

- Continuous quality improvement, Toyota “lean” production, Six Sigma, and failure mode and effects analysis are strategic tools for implementing QMS that are realizing benefits among early adopters, from small physician office laboratories to large reference laboratories. Use of continuous quality improvement and Six Sigma has contributed to financial savings and decreased turnaround time, lean production has improved test quality and reduced errors, and failure mode and effects analysis has decreased time to report critical laboratory values.
- To date, QMS has been most broadly adopted in transfusion medicine to meet Food and Drug Administration (FDA) requirements. However, adoption of QMS more broadly among laboratories should increase as CMS and accreditation organizations incorporate these standards into their requirements. Obstacles to implementation of QMS that must be addressed include resistance to culture change, lack of leadership and staff commitment to QMS, and insufficient funding of QMS activities.
- Aside from PT, CLIA provisions have emphasized structural policies, procedures, and documentation requirements as a condition for accreditation and certification. Process measures to assess quality in the TTP remain relatively underdeveloped. Existing ones have not been uniformly defined or assessed for generalizability, and are subject to wide variation in their implementation.
- Substantial work is needed to standardize indicators for pre- and postanalytic process-related performance measures. Data collection, analysis, and reporting methods also need to be standardized.
- Research on laboratory performance has been limited by its focus on the larger, hospital-based laboratories. Further research is needed examine the challenges faced by smaller laboratories and physician office laboratories when implementing process-related performance measurement and quality improvement programs.
- A small body of evidence addresses the downstream clinical and economic impacts of particular tests. The lack of substantive research on the impact of laboratory testing restrains the demonstration of the value of laboratory medicine.

LABORATORY INFORMATION SYSTEMS

Laboratory information systems (LIS) have evolved over the past 30 years from simple systems designed to generate accurate reports to complete systems that can link laboratory data “end to end” across the TTP. Information technology and Web-based applications have enabled dramatic

improvements in laboratory data management, communications, services, education, and marketing. Health care organizations have helped to advance the integration and reach of laboratories by linking the LIS with hospital information systems, pharmacy databases, etc.

- The extent of LIS adoption and capabilities varies widely. While integrated delivery systems and large laboratories rely on LISs for many aspects of laboratory testing, physician office laboratories and smaller laboratories primarily use the LIS to facilitate compliance with CLIA requirements (e.g., QC, PT, QA, patient test management).
- Lack of harmonized data standards is the single greatest barrier to laboratories' ability to integrate data within the laboratory as well as exchange data with external partners. Further progress in integrating laboratory data more fully with clinical practice applications cannot be realized unless laboratories, health care organizations, vendors, and others stakeholders resolve differences in data interchange and terminology standards.
- Successful integration of enhanced data management features requires increased computing power and multidirectional, coordinated communication that links the LIS, preanalytic processing components, specimen transportation system, analyzers, and postanalytic archiving system.
- The volume and complexity of data generated from genetic, proteomic, and pharmacogenetic testing, especially from high-throughput analyses and increased reliance on automation, requires that LISs be capable of storing and retrieving large quantities of data.
- Enabling CPOE, decision support systems, and electronic health record applications with laboratory data in real time requires continued development of rule-based algorithms capable of generating and integrating accurate alerts, reminders, order sets, results reports, and a list of differential diagnoses based on patient signs, symptoms, and characteristics.
- Digital pathology systems require further advances in high-power computation, data storage capacity, image formatting, and processing algorithms to facilitate the shift from single-field images to whole-tissue-processing.

FEDERAL REGULATORY OVERSIGHT OF LABORATORY MEDICINE

In the U.S. health care system, the purposes of regulation include one or more of the following: protect personal and public health, advance personal and public health, and ensure that the public has access to sufficient, accurate information for using regulated products and services to improve their health. The purpose of oversight by designated agencies and organizations is to enforce and otherwise achieve adherence to the rules and standards comprising regulation.

CLIA has served as the primary regulatory program governing U.S. clinical laboratory testing since its implementation in 1992. The CLIA program is administered by CMS, which has primary oversight of the program, in cooperation with CDC and FDA. Rapid technological advances, demographic shifts, lower tolerance for error, and higher expectations for personal data security pose challenges to certain aspects of the current regulatory framework for clinical laboratories.

- Technological advances have made laboratory tests easier to use and less subject to user error, resulting in considerable growth in the number of waived tests from 9 tests in 1993 to more than 1,600 test systems and 76 analytes in 2007. However, a CMS study found that

some certificate of waiver facilities perform tests beyond the approved level of complexity. CMS has taken measures to support surveys at a percentage of these facilities.

- For non-waived testing, available evidence on the long-term impact of PT on laboratory performance is limited, and findings of existing studies are confounded by limited comparable data from CMS and survey organizations and other methodological shortcomings. Existing studies indicate generally improved performance in recent years, although some failure rates remain unacceptably high.
- While laboratories' flexibility to self-determine QC procedures is desirable, several factors may contribute to the inconsistencies in implementing this practice. CMS, the Clinical and Laboratory and Standards Institute, and other stakeholders are developing evaluation protocols that will outline principles for validation and provide laboratories with scientific guidance on the development of QC procedures for specific testing technologies and environments.
- CMS has taken several actions to improve the operation of the program, including aligning CLIA technical requirements for QA, QC, and PT with systems-based approaches to quality management; issuing guidance documents identifying effective survey processes; strengthening enforcement of regulatory obligations; and assembling a working group to assess program expansion opportunities pertaining to revenues, staffing levels, and data collection capabilities.
- Only a small number of genetic tests are regulated as *in vitro* diagnostics subject to FDA premarket review for safety and efficacy (via the 510(k) or pre-market approval routes). Most genetic tests are developed in-house by laboratories and are regulated under CLIA general provisions. This framework may be insufficient for the level of efficacy and protection sought for many tests by clinicians and patients, and creates incentives for genetic tests to be categorized as laboratory-developed tests and not be subject to the 510(k) or premarket approval routes associated with FDA-regulated tests. CMS is working with the Secretary's Advisory Committee on Genetics, Health, and Society; CDC; CLIAC; FDA; and other experts to ensure the quality of genetic testing.
- Recent guidance documents issued by FDA clarify its oversight of *in vitro* diagnostic multivariate index assays and analyte specific reagents (the active ingredients used in some laboratory-developed tests). This guidance indicates a noteworthy assertion of oversight that exposes the small but growing area of highly complex genetic testing to greater scrutiny usually associated with premarket review processes.

REIMBURSEMENT FOR LABORATORY MEDICINE

Government and private sector third-party payment has enabled patients to access and benefit from health care products and services, including laboratory testing. The design and updating of coverage, coding, and payment systems should strive to enable patient access to medically necessary care, support delivery of high-quality care, and sustain innovation of new technologies. Further, these systems should discourage inefficiency, fraud and abuse, and non-competitive practices. Difficulty in acquiring coverage, appropriate coding, and adequate payment can pose significant hurdles in the use of laboratory testing and decreased incentives for laboratories and test manufacturers to engage in further test development.

Even though private sector insurance accounts for higher total revenues, the Medicare program exerts the strongest influence on laboratory services payment for all U.S. payers. All public payers and approximately 67% of private payers use Medicare's payment methodologies as the basis for their own and as tools for negotiating discounts with providers. Suboptimal practices and other shortcomings in the Medicare reimbursement system for laboratory testing affect other public and private sector payers in the U.S. health system. Redesign of the current Medicare payment system for laboratory services is needed in order to meet the growing scientific, technical, clinical, and economic challenges of the U.S. health care system.

- The Medicare statute restricts payment for screening and other preventive technologies and services, unless otherwise specified by Congress. Having to add these technologies and services to Medicare benefits on a case-by-case basis via the legislative route is cumbersome and impedes access to certain proven, beneficial tests.
- Continued use of 56 different fee schedules across the U.S. is inefficient and unnecessarily complex. For certain commonly ordered tests, the multiple schedules result in large regional variations, while for other tests, national limitation amounts results in inadequate Medicare payments.
- There is a notable lack of reliable data on the relationships among historical costs on which the Medicare Clinical Laboratory Fee Schedule is based, current production costs, and the effects of economies of scale and other cost-reducing effects of technological changes.
- Studies of data-derived methods for evaluating the appropriateness of payment rates and for designing potential new payment systems, e.g., based on resource-based relative value and microcosting (e.g., activity-based costing) have not been completed.
- CMS is proceeding with a competitive bidding demonstration project for laboratory services, with the expectation of substantial savings. Supporters of the demonstration believe that current prices on the fee schedule have no substantial relationship to actual costs. However, the demonstration project model is highly exclusive^a and could have significant detrimental effects on clinical laboratories that lose in the bidding process, as many depend on Medicare reimbursement for a sizable portion of their revenues.
- Despite modest improvements in their transparency, the processes for establishing payment levels for new laboratory tests, including assignment of new and existing Current Procedural Terminology® codes to tests and related methods of cross-walking and gap-filling, remain archaic and inadequate.
- Federal government investigations of clinical laboratory-related fraud and abuse resulted in penalties amounting to more than \$1.727 billion from 1992 to 2006. Through a separate rulemaking, CMS will address contractual joint ventures that enable non-pathologist physicians and other entities to profit from self-referrals of pathology services.

Approaching the close of the first decade of the 21st century, health care now accounts for one-sixth of the U.S. economy. Laboratory medicine guides, and is often the pivotal determinant in, decisions

^a Competitive bidding initiatives that rely on exclusive or selecting contracting allow only those laboratories submitting winning bids to participate; losing laboratories are barred from receiving any payment from contracts during the time of the procurement.

that influence the magnitude and allocation of resources in much of this burgeoning sector. Any efforts to improve the quality of health care, let alone transform it, must engage the vibrant market of laboratory medicine and its workforce, systems for ensuring quality, systems for managing information, and scientific and technological advances. Such efforts must also confront complex and, in certain ways, inadequate regulatory and payment systems that strain to cope with the extraordinary diversity and volume of this field. Further, it will be incumbent upon those in laboratory medicine to demonstrate its value continually along the dimensions of access, informed decisions, patient and provider satisfaction, health care outcomes, and cost-effectiveness.

INTRODUCTION

The history of laboratory medicine extends to the first recorded examination of human bodily fluids during the time of the ancient Greek physician Hippocrates around 300 BC.¹ Two thousand years later, the first true clinical laboratory opened in 1896 at Johns Hopkins Hospital.² Discovery of the disease-causing agents of epidemics such as tuberculosis, diphtheria, and cholera and the development of tests to detect their presence throughout the end of the 19th century propelled the laboratory to a position of importance by the early 20th century.³ The American Society of Clinical Pathologists was formed in 1922 as the first professional society supporting physicians specializing in pathology. In 1926, all hospitals accredited by the American College of Surgeons were required to establish a clinical laboratory under the direction of a physician.

Today, the clinical laboratory serves a vital role in the health care system, spanning research, clinical care, and public health surveillance. More than 200,000 clinical laboratories provide testing and services in the U.S. The Clinical Laboratory Improvement Amendments (CLIA) of 1988, consolidated regulation of all types of clinical laboratories under one statute and established standards for quality assurance, record maintenance, and proficiency testing for all laboratories. CLIA defines a clinical laboratory as:

“...a facility for the biological, microbiological, serological, chemical, immunohematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings. These examinations also include procedures to determine, measure, or otherwise describe the presence or absence of various substances or organisms in the body. Facilities only collecting or preparing specimens (or both) or only serving as a mailing service and not performing testing are not considered laboratories.”⁴

While this definition describes components of laboratory medicine and the activities that take place within a clinical laboratory, it does not fully address the *practice* of laboratory medicine. The practice of laboratory medicine implies a broader scope of influence beyond the activities in the laboratory, such as consultations with clinicians to assist with test ordering and results interpretation, performance measurement for quality improvement in the delivery of patient care, and, on a small yet growing scale, direct interactions with patients and the public. During a 1986 meeting of the Center for Disease Control and Prevention’s (CDC) Institute on Critical Issues in Health Laboratory Practice, the extralaboratory functions were incorporated into the concept of the total testing process—a framework defined by the activities of three distinct phases—preanalytic, analytic, and postanalytic—that align with clinical workflow outside and inside the laboratory. In 2003, CLIA provisions were revised to align regulatory requirements correspond with one total testing process. Thus, for the purposes of this report, laboratory medicine is defined broadly as:

Testing services and associated practices for the assessment, diagnosis, treatment, management, or prevention of health-related conditions utilized in making patient care decisions and improving public health.

CONTEXT OF THE REPORT

Although the U.S. ranks highest in per capita health care spending, there is overwhelming evidence of gaps between well-founded standards of care and health care practice.⁵ The Institute of Medicine (IOM) reports *To Err is Human: Building a Safer Health System* (1999) and *Crossing the Quality Chasm: A New Health System for the 21st Century* (2001), as well as other sentinel studies, have focused national attention on improving the quality and safety of care delivery.⁵⁻⁸ Stakeholders agree that the quality of care delivered in the U.S. is inadequate and that the organization and delivery of health care must be changed.

Given the shortfalls in quality and continued escalation in costs, health care must be assessed continually to inform decision-making, and redesign delivery and incentives as needed, to yield appropriate, high quality care. An integral component of care is laboratory medicine, which extends across research, clinical (i.e., screening, diagnosis, and treatment), and public health settings. Laboratory services account for only 2.3% of total health care expenditures; however, they have a significant role in informing health care decisions and spending. Appropriate use of laboratory testing is essential for achieving safe, effective, and efficient care to patients.

SCOPE OF REPORT

Health care must be informed by data derived from scientific assessment of efficacy and effectiveness of procedures, and must adapt to rapid changes in science, technology, and practice.⁹ Indeed, laboratory medicine is not only responding to these changes, but is contributing to them in an environment of demographic, social, and economic change. Detailed, comprehensive information about the laboratory medicine sector, particularly in regard to best practices and the quality of services provided, is necessary to address current and forthcoming challenges to this important aspect of health care.

CDC has commissioned this report, among others, to lay the groundwork for transforming laboratory medicine over the next decade. The Lewin Group, under subcontract to Battelle Memorial Institute, was charged with drafting this document, *Laboratory Medicine: A National Status Report*. The report provides a detailed overview of the key factors affecting the laboratory medicine sector. It is intended that the report serve as a point of reference for measuring and improving quality in the future as well as for policy guidance to professional organizations, government agencies, and others who provide, use, regulate, and pay for laboratory services. Aside from an executive summary and this introduction, the report is organized as follows:

- **Chapter I** describes the value of laboratory medicine in clinical care and the broader health care system. The chapter addresses the roles of laboratory medicine in screening, diagnosis, and treatment; evidence-based medicine; clinical practice guidelines; assessing quality of care; contributing to cost-effective health care; and protection from threats to public health.
- **Chapter II** provides detailed information on the magnitude and composition of the U.S. clinical laboratory testing market, including data by setting (hospitals, physician offices, independent laboratories, home), and by clinical discipline (clinical pathology, including molecular diagnostics; anatomic pathology).

- **Chapter III** provides an overview of the laboratory medicine workforce, including professional responsibilities, demographic characteristics, vacancy rates, and wages. The chapter also addresses the status of educational programs and licensing and certification requirements at the federal and state levels.
- **Chapter IV** describes the total testing process and the quality issues and errors most relevant to each phase of laboratory testing for clinical and anatomic pathology. Also addressed are communication factors associated with the preanalytic and postanalytic phases. A section of the chapter examines point-of-care testing and related matters of quality.
- **Chapter V** describes the status and future of quality systems in laboratory medicine, including the shift away from analytic-focused quality control, quality assurance, and proficiency testing to more comprehensive, systematic approaches to quality management. Also included is discussion of the current status of performance measurement in laboratory medicine.
- **Chapter IV** addresses laboratory information systems and automation technology, including the extent to which they have been adopted into integrated delivery systems and physician office laboratories. This includes discussion of emerging technologies (e.g., computerized physician order entry, electronic health records) and health care system integration requirements.
- **Chapter VII** describes federal regulatory oversight of clinical laboratories by the Centers for Medicare and Medicaid Services (CMS)^a and oversight of marketed tests by the Food and Drug Administration (FDA). The chapter reports on the status of waived testing, the status of non-waived testing under CLIA (e.g., proficiency testing, quality control, personnel, and surveys), the respective roles of CMS and FDA in oversight of laboratory developed tests, and outstanding issues in genetic testing and transfusion medicine.
- **Chapter VIII** describes public and private sector reimbursement systems for clinical laboratory services, with a focus on coverage decisions, coding and payment methodologies associated with prospective and fee-for-service systems, and new initiatives to reduce costs, such as competitive bidding.

^a Formerly, CMS was the Health Care Financing Administration.

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METHODS AND LIMITATIONS

The process for development, organization, and management of the report content is summarized in this section. Also briefly discussed are certain limitations of available data and information used in the report.

METHODS

Report Outline

A kick-off meeting was held in October 2006 in Atlanta to review the purposes and scope of this report and other tasks associated with the broader contract. CDC, Battelle, and invited experts provided background information on key aspects and issues in laboratory medicine to be considered for inclusion in the status report. Drawing from the meeting, Lewin drafted an outline of the structure and content of the report. The outline was circulated to the representatives of laboratory medicine stakeholder groups for review and comment. Suggested modifications were considered and incorporated as appropriate. As Lewin initiated the report, assembled information, and gained further insights from experts and other stakeholders, the scope of the report was refined further under the guidance of a Technical Experts Committee.

Technical Experts Committee

In January 2007, nine individuals agreed to serve on the multidisciplinary Technical Experts Committee. The committee members were selected and approved by CDC on the basis of their experience, interest, and expertise in one or more of the main topic areas addressed by the report. They functioned as advisors, providing guidance on the development of specific chapters to ensure that the report content was comprehensive, appropriate, and accurate. Members of the committee provided input on specific queries and document drafts via conference calls and electronic communications.

Data Gathering

In preparing this report, Lewin compiled, analyzed, and synthesized secondary data from multiple sources, including published and unpublished literature, government databases and reports, market research reports, Internet searches, and personal communications with industry experts and government officials.

Literature searches

For a broad environmental scan of the field, Lewin conducted searches of published and unpublished literature using bibliographic databases and web-based search engines. In the peer-reviewed journal literature, searches were conducted predominately in the MEDLINE/PubMed database. This involved examination of qualitative and quantitative literature covering general and systematic reviews, guidelines, clinical trials, observational studies, and other analyses. For specific sections of the report, searches also were conducted in the Cochrane Library, National Guideline Clearinghouse, and Blue Cross Blue Shield Technology Evaluation Center Assessments database.

Government database searches and reports

The Online Survey, Certification, and Reporting (OSCAR) database of CMS provided information about laboratory certification, accreditation, and proficiency testing. Queries of the OSCAR database produced the most recent estimates of test volume for waived and non-waived tests by laboratory setting and numbers of facilities performing waived and non-waived tests. Searches of publicly available CMS databases, such as those for the Medicare Physician Fee Schedule, Clinical Laboratory Fee Schedule database, and Part B Extract Summary System Data File, provided information about payment rates.

Numerous federal government sources, including public notices, regulations, guidances, conference proceedings, and other reports, yielded other essential information. Resources were used from the spectrum of Department of Health and Human Services (DHHS) agencies and advisory committees, including the Agency for Healthcare Research and Quality (AHRQ)^a; CDC; CMS; Clinical Laboratory Improvement Advisory Committee (CLIAC); Health Research and Services Administration; FDA; DHHS Office of the Inspector General (OIG); Office of the National Coordinator for Health Information Technology; and the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS). Federal agencies that provided additional useful information included the Bureau of the Census, Bureau of Labor Statistics, Government Accountability Office (GAO)^b; Office of Management and Budget; Department of Defense (DoD); Veterans Administration; Department of Justice; Securities and Exchange Commission; and The White House. Information at the state level was obtained from state departments of health.

Market research reports

Market research reports and newsletters provided key information about market trends, workforce, technological advances, and other aspects. Particularly relevant were those from Washington G-2 Reports, including *Lab Industry Strategic Outlook: Market Trends and Analysis 2007* and *Laboratory Market Leaders Report 2008*, which drew from extensive survey data, CMS and other agency data, financial reports filed with the SEC, Bureau of the Census data, and expert interviews. Also useful were Washington G-2 Reports newsletters, e.g., the *Laboratory Industry Report*, *Diagnostic Testing and Technology Report*, *G-2 Compliance Report*, and *National Intelligence Report*. Supplying further data on the laboratory medicine market, regulation, new technology, and related trends were Knowledge Source Inc.'s *Clinical Laboratory Testing Market Overview 2006* and Kalorama Information's *Molecular Diagnostics: Major World Markets* (2007).

Internet searches

Along with literature sources, Lewin used Internet search engines to gather web-based information on particular topics. This included information posted by public and private sector organizations involved in the laboratory medicine and health care community, such as government agencies, accreditation organizations, professional societies, industry associations, standards organizations, research organizations, academic institutions, medical centers, manufacturers, and international public policy organizations. Resources from these organizations were evidence-based where applicable, current, and relevant to topics addressed in the report.

^a AHRQ was formerly the Agency for Health Care Policy and Research.

^b GAO was formerly the General Accounting Office.

Personal communications

For clarification of important concepts or to gather information where literature or data sets were lacking, Lewin relied on personal communications with experts in industry, professional groups, government agencies, and other public and private sector organizations.

LIMITATIONS

Our extensive search of the sources described above did encounter certain gaps and other limitations. First, publicly available information about the economic status and quality of the laboratory medicine sector is patchy, inconsistent, and of uneven quality. Although the OSCAR database contains the most extensive set of industry data, there is no standardized mechanism for estimating such important parameters as volume for panel tests. The lack of standardization, coupled with self-reported, irregular data collection by laboratories, results in gaps and inconsistencies in estimates of test volumes, spending on services, and market revenue. This limits determinations of long-term trends and market value for laboratory testing and services. In addition, the inability of those outside CMS to directly query the OSCAR database further complicated the research process. In terms of the market research reports, data from surveys was limited due to low response rates. For example, one of the surveys conducted for the 2007 report was sent to 12,000 laboratories in their database but only 141 responded. Such data could benefit from efforts to obtain higher response rates.

Second, lack of data standardization confounds comparability of published study findings regarding laboratory quality and error rates. Formal measurement and reporting on quality has been limited largely to analytic-related processes. Data collection in studies examining preanalytic and postanalytic factors has been insufficiently standardized across participating providers and laboratories. Many of the quality indicators used for the studies (e.g., specimen labeling/identification) have not been adequately validated. This contributes to wide ranges in estimates of errors, and generally inconsistent quality measurement across these institutions.

Third, understanding of the current status of laboratory medicine is constrained by the lack of research on many important aspects of the field. For example, there are very few studies of laboratory practice outside the hospital setting (e.g., physician office laboratories), although the majority of clinical care takes place in the ambulatory care setting. There is a notable lack of research on the needs of specific populations, such as pediatric patients, frail elderly patients, and those with multiple chronic conditions, as most published studies involve the non-elderly adult population and typically focus on a single health issue, e.g., diabetes. Research also is underdeveloped on the relationship of laboratory services to patient outcomes and cost of care. Fortunately, there is growing recognition of the importance of such research. Lastly, there is a notable lack of reliable data on the relationships among historical costs on which payment is based, costs of providing laboratory testing, what constitutes payment adequacy, and the effects of economies of scale and other cost-reducing effects of technological changes. These limitations curtail understanding of important aspects of laboratory medicine related to the quality of services in physician office laboratories, quality of care for specific patient groups, trends in population health, and the efficiency and value of laboratory services within the broader health care system.

CHAPTER I

THE VALUE OF LABORATORY MEDICINE TO HEALTH CARE

Laboratory medicine is an essential element of the health care system. It is integral to many clinical decisions, providing physicians, nurses, and other health care providers with often pivotal information for prevention, diagnosis, treatment, and management of disease.¹ Laboratory tests and services supply clinicians with information necessary to provide high quality, safe, effective, and appropriate care to patients. The key role of laboratory testing is reflected in evidence-based medicine (EBM) and clinical practice guidelines. Health care providers, quality assurance organizations, and payers are incorporating selected laboratory tests into indicators to objectively assess quality of care for individual patients and populations and to support payment policies.

Laboratory medicine has an essential role in risk management. Not only can testing help to prevent certain adverse events, it can facilitate detection and recovery from adverse health events when they do occur. Laboratory tests help to prevent infectious agents from getting into the blood supply and ensure the safety of organs and tissues for transplant. Through effective and timely surveillance, tests can help to mitigate threats to patient and population health (e.g., influenza, nosocomial infections, severe acute respiratory syndrome).

The contributions of laboratory tests and services as an essential component and partner in health systems remain under-recognized. Despite the extensive role of laboratory medicine in informing medical decision-making, spending on laboratory services accounts for only 2.3% of national health care spending and 2% of Medicare expenditures.^{1,2} As overall expenditures on health care continue to rise, appropriate use of laboratory tests can facilitate cost-effective care via early detection and improved management of priority health conditions. Recent and emerging technological advances gained from mapping the human genome, including applications of genetic testing that enable personalized medicine, call greater attention to the contributions of laboratory medicine to patient care as well as the scientific and medical knowledge base. This chapter summarizes the value of laboratory medicine to health care and patient and population health.

VALUE TO THE QUALITY OF PATIENT CARE

Despite the world's highest per capita spending on health care, there is overwhelming evidence in the U.S. of gaps between well-founded standards of care and its actual delivery. Among the main factors often cited to explain deficiencies in quality are:

- Growing complexity of science and technology, some of which has advanced more rapidly than our ability to integrate it into safe, effective, and efficient health care
- Longer life expectancy, which has significantly increased the chronic disease burden and the resources being devoted to chronic disease care
- A highly decentralized health care system that is often bureaucratic, wasteful, and difficult to navigate
- Underinvestment and disparities in access to health information technology, constraining the ability of technology to improve the quality of care³

Health care stakeholders concur that the quality of care delivered in the U.S. is inadequate and that its organization and delivery must be fundamentally changed. The IOM reports, *To Err is Human: Building a Safer Health System* (1999) and *Crossing the Quality Chasm: A New Health System for the 21st Century* (2001), and other sentinel studies such as the RAND report on the *Quality of Health Care Delivered to Adults in the U.S.* (2003) have helped to mobilize national action on prevention of medical errors and quality improvement.³⁻⁶

Public and private sector efforts to redesign and improve the health care delivery system are grounded in the six aims of quality identified by the IOM: safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity.⁵ Using these dimensions of quality, health care organizations, professional groups, private and public purchasers, and others are developing specific policies, practices, and measures for each element, with the overarching goals of diminishing illness, injury, and disability as well as increasing the health and function of the U.S. population. Examples of how laboratory medicine supports each of the six aims are provided below.

- **Safety** refers to protection of patients from harm due to care that is intended to help them and protection of health care workers from harm while providing care.³ Laboratory medicine contributes to diminishing the risk of harm when patients and specimens are accurately identified, specimens are collected appropriately, measures are taken to prevent specimen contamination, process control measures are executed during analytic processes, and test results are complete and understandable.⁷
- **Effectiveness** refers to measures of how well health care interventions (screening, diagnosis, treatment, etc.) achieve their intended outcomes or other impacts.³ Laboratory medicine supports effectiveness when test ordering is evidence-based, specimen collection follows science-based procedures, specimen analysis and results reporting conform to well-established standards, and testing results in improved patient outcomes.⁷
- **Patient-centered** care is respectful of and responsive to individual patient values, preferences, and expressed needs, and ensures that patient values guide decision making.⁸ Laboratory medicine supports patient-centered care when test ordering reflects patient preferences, including end-of-life care, specimen collection is designed for patient comfort and satisfaction, and test results are understandable to and actionable by the patient and clinician. These attributes can contribute to favorable patient experience of the health system and quality of care.
- **Timeliness** of care minimizes, unnecessary delays that can result in emotional or physical harm.^{3,9} Timely transport of specimens, decreased turnaround times (TATs) in routine and stat^a testing, and timely notification of critical or abnormal values are primary ways that laboratories support quality of care.^{7,10}
- **Efficiency** refers to using resources to optimize production of desired results.³ Laboratory medicine contributes to health care efficiency when waste is eliminated or reduced, including that associated with inappropriate test ordering (e.g., underuse,

^a Stat testing refers to laboratory tests for which results are needed as quickly as possible and which are given priority by laboratories.

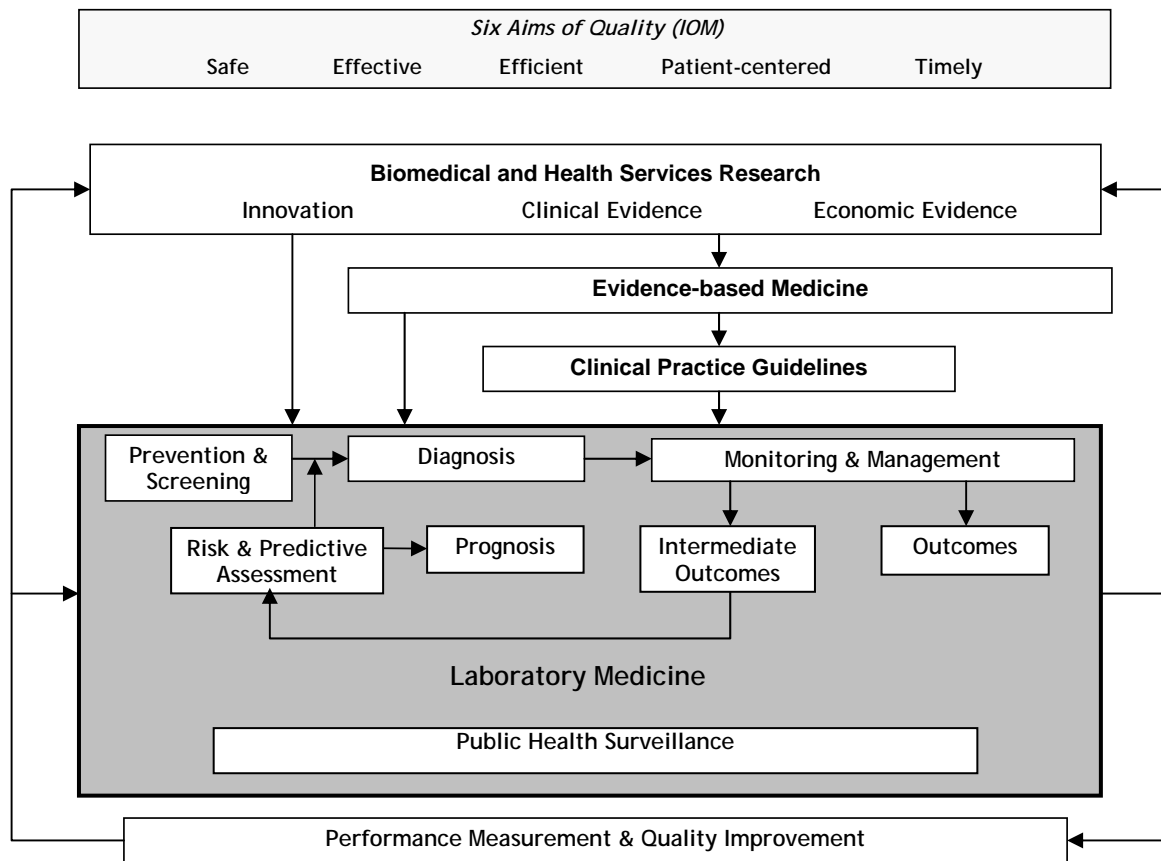
overuse, and misuse), redraws or recollection of specimens, repeating specimen analysis, and correcting inaccurately documented test results.⁷

- **Equity** of care ensures that quality does not vary because of patient personal characteristics such as sex, race/ethnicity, geographic location, or socioeconomic status.³ Laboratories contribute to equitable care when they provide services in a manner that is unbiased, accommodate the special needs of patients during specimen collection, use reference intervals that account for population differences, and present information according to the language and literacy level of the patient.⁷

Figure 1.1 portrays the dynamic role of laboratory medicine in the health care system. This diagram has as its premise that value can be expressed in terms of achieving the six aims posed by the IOM.

Laboratory indicators also provide a means to assess quality of care. Test use as indicated by clinical practice guidelines and related protocols, as well as test results themselves, are being incorporated into indicators of provider performance and health care quality. Clinical laboratories facilitate collection, analysis, and interpretation of data at the individual and population levels that are necessary for ensuring the public health, such as monitoring rates of nosocomial infections, development of drug resistance, infectious disease outbreaks, and biological and chemical threats.

Figure 1.1: Value of Laboratory Medicine to the Health Care System



VALUE TO EVIDENCE-BASED MEDICINE

Though its antecedents extend to the mid-19th century, the widespread practice of EBM and its broader, yet not universal, acceptance in the U.S. is a more recent development spanning the past two decades. EBM is commonly defined as the explicit use of best evidence in decision-making about the medical care of individual patients.^{11, 12} EBM derives from thorough, well-founded methods and resources for generating evidence, including the use of randomized controlled trials and other rigorous study designs as appropriate; use of meta-analyses, systematic reviews, and other structured approaches for integrating evidence from multiple sources; and standardized reporting of research results.¹³ In general, EBM is based on five main principles:

- Decisions about health should be based on the best patient-, population-, and laboratory-based evidence
- The problem determines the most appropriate source of evidence
- The best evidence is identified by integrating epidemiological, biostatistical, and pathophysiological methods with personal experience
- The value of searching for and appraising evidence is derived from translating evidence into actions that affect patients
- The ways in which these principles are carried out and performed must be continuously evaluated¹⁴

Laboratory testing plays a major role in supporting EBM in clinical practice. As described in greater detail below, EBM increasingly informs the development of clinical practice guidelines.¹³ The hemoglobin A1c (HbA1c) test, which measures the amount of glucose bound to hemoglobin, allows clinicians to monitor the average amount of glucose in a patient's blood over the previous two to three months.¹⁵ Based on results of HbA1c testing in clinical trials such as the Diabetes Control and Complications Trial, a large randomized controlled clinical trial that involved more than 1,400 type 1 diabetic patients, researchers were able to assess glucose levels and determine optimal treatment protocols for individuals with this condition.¹⁶

VALUE TO CLINICAL PRACTICE GUIDELINES FOR PATIENT CARE

Clinical practice guidelines are systematically-developed statements intended to assist practitioners and patients in making decisions about health care in specific clinical and personal circumstances.¹⁷ While clinicians have long used such means as treatment recommendations, immunization schedules, practice bulletins, and algorithms to inform decision-making, clinical practice guidelines focus on summarizing research and external evidence to develop recommendations.¹⁸ This more rigorous approach typically involves a multidisciplinary team that reviews some systematic compilation of relevant evidence, working according to explicitly described methods.^{19, 20}

Among the factors underlying variation in clinical practice are overuse, underuse, and misuse of health care interventions.^{13, 21} Clinical practice guidelines are intended to reduce this variation and improve the quality, safety, efficiency, and effectiveness of clinical care. Guidelines have been developed for nearly all facets of medical care, spanning prevention,

surveillance, diagnosis, treatment, monitoring, rehabilitation, and palliation; and applying to drugs, devices, procedures, and systems.^{13, 19}

Quality indicators increasingly are incorporating laboratory testing. For example, 102 (23%) of the 439 quality indicators assessed in the RAND analysis of the quality of care delivered to U.S. adults involved diagnostic tests.⁴ The 2006 *National Healthcare Quality Report* from AHRQ includes eight clinical conditions, seven of which involve laboratory testing: end-stage renal disease, colorectal cancer, diabetes, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), mental health/substance abuse, heart disease, and pneumonia.²² In a study conducted by The Lewin Group in 2005, a search of the National Guideline Clearinghouse and MEDLINE was undertaken to estimate the extent to which laboratory tests were included as part of evidence-based clinical practice guidelines across the 23 main condition/disease categories defined by the National Guideline Clearinghouse. Of 1,230 guidelines identified, 460 (37%) focused on or involved laboratory tests.

Table 1.1 outlines priority health conditions identified in these sources and corresponding estimates of the prevalence and spending on each. For each health condition, common laboratory tests used in screening, diagnosis, and/or monitoring are shown.

Table 1.1: Sample of Priority Health Conditions, Associated Laboratory Tests, Prevalence, and Cost to the Health System

Health condition	Examples of laboratory tests used in diagnosis and/or patient management	Number of Americans Affected	Spending on Condition
Heart disease	Lipid panel, troponin	79.4 million (2004) ^a	\$403 billion (2006) ^b
Respiratory disease ^l	Blood gas test, bacterial culture, viral culture	15.7 million ^{ll} (asthma); 1.3 million ^{lll} (pneumonia) ^{c, d}	\$144.2 billion (2006) ^b
Cervical cancer	Pap smear, human papillomavirus DNA testing	11,150 cervical cancer diagnoses (2007) ^e	\$1.7 billion (2004)
Colorectal cancer	Fecal-occult blood test	112,340 colon cancer diagnoses (2007) ^e	\$8.4 billion (2004) ^f
Diabetes	Glucose, HbA1c	20.8 million (2005) ^g	\$132 billion (2002) ^g
End-stage renal disease	Creatinine, BUN	472,000 (2004) ^h	\$32.5 billion (2004) ^h
HIV/AIDS	Antibody testing, CD4 testing, RNA	1.2 million (2006) ⁱ	\$21.1 billion (2006) ⁱ
Maternal health (prenatal care)	Blood and Rh type with antibody screen	83.9% pregnant women began prenatal care in first trimester; 3.6% began prenatal care in third trimester or not at all (2004) ^j	\$26.2 billion (2005) ^k
Mental health/substance abuse	Drug tests, liver function	24.6 million adults ^{lv} (classified with serious psychological distress) (2005); 22.2 million people ^v (classified with substance dependence or abuse) (2005) ^l	\$104 billion (2001) ^m
Influenza	Viral culture, serology, rapid antigen testing	5-20% of the U.S. population is infected with the influenza virus each year ⁿ	\$200 on treatment per infected person (2003) ^o
Health care-associated infections	Viral culture, molecular typing of microbial pathogens	1.7 million (2006) ^p	\$10,500-\$111,000 per case (2004) ^p

Based on review of the National Guideline Clearinghouse, Agency for Healthcare Research and Quality, and Medline, National Library of Medicine. Tests identified from Lab Tests Online.

^IIncludes, but is not limited to, severe asthma and pneumonia

^{II}Indicates number of non-institutionalized adults

^{III}Indicates number of discharged patients

^{IV}Includes people aged 12 and older

^VIncludes people aged 18 and older

^aRosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2007;115(5):e69-171.

^bFact book fiscal year 2005. Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health, 2006.

^cFaststats: asthma. Hyattsville, MD: National Center for Health Statistics, 2007.

^dFastats: pneumonia. Hyattsville, MD: National Center for Health Statistics, 2007.

^eCancer facts and figures 2007. Atlanta, GA: American Cancer Society, 2007.

^fCancer trends progress report--2005 update. Bethesda, MD: National Cancer Institute, National Institutes of Health, 2005.

^gNational diabetes statistics fact sheet: general information and national estimates on diabetes in the United States, 2005. Bethesda, MD: National Diabetes Information Clearinghouse, National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health, 2005.

^hU.S. Renal Data System, USRDS 2006 annual data report: atlas of end-stage renal disease in the United States. Bethesda, MD: National Institutes of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2006.

ⁱHIV/AIDS policy fact sheet. Menlo Park, CA: Kaiser Family Foundation, 2006.

^jHealth, United States, 2006 with chartbook on trends in the health of Americans. Hyattsville, MD: National Center for Health Statistics, 2006.

^kInstitute of Medicine. Preterm birth: causes, consequences, and prevention. Washington, DC: National Academy Press, 2006.

^lResults from the 2005 National Survey on Drug Use and Health: national findings. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2006.

^mMark T, Coffey RM, McKusick T, et al. National expenditures for mental health services and substance abuse treatment, 1991-2001. Rockville, MD: S Center for Substance Abuse Treatment, Center for Mental Health Services, Substance Abuse and Mental Health Services Administration, 2005.

ⁿKey facts about influenza and the influenza vaccine. Atlanta, GA: Centers for Disease Control and Prevention, 2007.

^oSoni A, Hill SC. Average annual health care use and expenses for influenza, 2001-2003. Statistical brief #116. Rockville, MD: Agency for Healthcare Research and Quality, 2006.

^pStatement by Denise Cardo, MD, Director, Division of Healthcare Quality Promotion, National Center for Infectious Diseases, Centers for Disease Control and Prevention, on CDC's role in monitoring and preventing healthcare-associated infections before the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce, 109th Congress, 2nd session. 2006.

VALUE OF LABORATORY TESTS AND SERVICES ACROSS PATIENT CARE CONTINUUM

Laboratory medicine provides value across the continuum of patient care. In addition to providing objective data about patient health, laboratory medicine enables early assessment of disease risk, use of preventive and less invasive treatment, selection of appropriate treatment, and monitoring treatment. Used appropriately to inform patient management decisions, laboratory testing can contribute to optimizing use of health care resources and decrease short-, medium-, and long-term costs of care.²³

Screening for Risk Factors of Developing Specific Disorders

Screening tests may be conducted on asymptomatic individuals to check for risk factors and other indicators of developing or latent disease.²⁴ Especially for children and young adults, such testing can avoid or diminish the impact of diseases and medical conditions that appear later in life. Screening tests for adults can detect certain common diseases that, when identified early, can be more easily treated.^{25, 26}

Access to preventive and screening laboratory testing services in the U.S. varies. Although Medicare's authorizing legislation (Title XVIII of the Social Security Act) excludes coverage for preventive interventions and diagnostic laboratory tests for asymptomatic individuals, Congress has mandated Medicare coverage of selected screening and diagnostic procedures over the years. Pursuant to the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), preventive benefits provided by Medicare effective in 2005 include a "Welcome to Medicare" physical exam and screening for heart disease and diabetes, along with earlier mandated tests for osteoporosis, glaucoma, and cancers of the colon, breast, cervix, and prostate.^{27, 28}

The disparities between insured and uninsured people in the U.S. in access to care extend to laboratory testing. Compared to adults with any type of health insurance coverage, uninsured adults in the U.S. are less likely to receive preventive and screening services at all and are less likely to receive these services on a timely basis.²⁹ People in the U.S. who are uninsured are more likely to report duplication of laboratory tests, laboratory test errors, and delays in receiving laboratory test results.³⁰

Screening to Determine Individual Risk

Genetic testing involves analysis of human deoxyribonucleic acid (DNA), ribonucleic acid (RNA), chromosomes, proteins, or certain metabolites to detect genetic alterations related to a heritable medical disorder.³¹ A universal definition of genetic testing has not been recognized by regulatory or professional bodies. SACGHS defines a genetic test as one that involves the analysis of chromosomes, DNA, ribonucleic acid, genes, or gene products to detect heritable or somatic variations related to genes or health.³² In its draft 2007 report on oversight of genetic testing, SACGHS calls on relevant agencies to develop an appropriate definition of health-related genetic tests.

Genetic testing can be used to determine whether an individual is a carrier for a disease or condition or has a heightened risk of developing a disease years or decades later.³³ It also can be used for diagnostic or prognostic purposes and as a predictive tool to assess an individual's drug metabolism. The main types of genetic testing include the following:

- Carrier identification is used to determine whether an individual possesses a potentially harmful gene that can be passed on to progeny. Prenatal/maternal serum screening is used to determine whether a fetus is at risk of having specific genetic conditions and to detect open neural tube defects and certain chromosomal abnormalities. Current prenatal diagnosis is targeted at specific diseases and/or mutations rather than determining the general genetic make-up of the fetus.
- Newborn screening is most often used to determine whether a newborn has a medical condition that requires immediate treatment, e.g., phenylketonuria, congenital hypothyroidism.
- Late-onset disorder testing is used to determine an adult's susceptibility or predisposition to complex diseases (e.g., cancer, heart disease, Huntington's disease).

The increasing role of genetic testing is due in great measure to advances in understanding the role of genetics and molecular biology in disease development. Genetic tests are now available for more than 1,400 diseases.³⁴ Tests for an estimated 287 of these diseases are being used only in research settings. Many diseases are known or thought to be caused by inherited or spontaneous

acquired DNA alterations, e.g., Down syndrome, Huntington disease, sickle cell anemia, and hemophilia, and thought to cause or contribute to many others, including Alzheimer's disease, breast cancer, leukemia, and osteoarthritis.³⁵ Genetic testing for early-onset Alzheimer's disease detects mutations in three single genes that are understood to lead to the development of the disease at an early age, typically before the age of 60.³⁶ Breast cancer (BRCA) gene analysis, which is often performed by sequencing the *BRCA1* and *BRCA2* genes, identifies mutations in these two genes that are associated with predisposition to breast and ovarian cancer. *BRCA1* and *BRCA2* mutations have been identified in 1-2% of women diagnosed with breast cancer and 5-10% of women diagnosed with ovarian cancer.³⁷

Diagnosing Conditions and Evaluating Prognosis

Early detection

Laboratory tests are critically important for accurately diagnosing a disease in its earliest stages, determining disease severity, assessing the likelihood of recovery, and evaluating the potential for adverse outcomes. Accurate and early diagnosis allows clinicians and patients to better evaluate the benefits and risks of various treatment options, begin treatment promptly and, in the case of contagious conditions, prevent a disease from spreading to others. Laboratory tests are used by clinicians and, increasingly, patients, to inform prevention and treatment decisions and related courses of action.

Early-stage detection via laboratory testing is established for such diseases and conditions as breast cancer, cervical cancer, skin cancer, thyroid dysfunction, high cholesterol, and diabetes. Using the Papanicolaou test (Pap test or Pap smear), a pathologist or cytotechnologist can identify cervical cells that are cancerous or potentially pre-cancerous.³⁸ The American Cancer Society, U.S. Preventive Services Task Force (USPSTF), and American College of Obstetricians and Gynecologists recommend that young women receive Pap tests every year beginning no later than age 21; women over the age of 30 who have no new risk factors and who have had normal results for three consecutive years are advised to get retested every two-to-three years. Broad use of the Pap test as a screening tool to detect pre-invasive lesions is credited with reduction in the annual incidence rate (from 14.8 to 7.0 per 100,000) and mortality rate (from 5.6 to 2.4 per 100,000) of malignant cervical cancer in the U.S. between 1975 to 2004.³⁹⁻⁴¹

When diseases are identified at an early stage or before symptoms have appeared, patients and their health care providers can take measures to prevent or reduce the risk of developing the disease or condition, including increased medical monitoring, lifestyle changes and, when needed, medical interventions.³⁷ Similarly, early measures may minimize the severity of the disease and its effects on mortality, morbidity, and quality of life. These measures also can diminish downstream health care spending that would have been caused by the disease. For instance, early detection of incipient colorectal cancer (e.g., using fecal-occult blood testing) is associated with more successful treatment and increased survival.⁴²

Diagnosis

Along with an individual's signs, symptoms, personal history, and family history, laboratory tests are used to arrive at or eliminate possible diagnoses.⁴³ A laboratory test used for "ruling in" a disease or condition indicates that it may be present if the test results are abnormal. "Ruling out"

a disease or a condition allows the clinician to consider alternative diagnoses and make more efficient use of resources.

Laboratory tests can be used to determine the degree to which the disease has progressed and the severity of the disease. Laboratory tests, including studies of blood, urine, other bodily fluids, and bodily tissues play a major role in the “staging” of cancer and other diseases, i.e., describing the severity of a disease based on the extent to which it has spread throughout the body.⁴⁴ Tests to determine the extent and severity of a disease can be the same or different from those for diagnosis. For example, measurements of HbA1c and glucose are used to diagnose diabetes and to monitor diabetic individuals.⁴⁵

Among other examples, laboratory tests can direct a diagnosis in the case of pharyngitis, or inflammation of the pharynx, which can be caused by a variety of microorganisms.⁴⁶ Group A streptococcus (GAS) is a bacterial cause of pharyngitis and can be treated with antibiotics. Only about 15% of sore throats are caused by GAS; therefore, the results of a streptococcal screen provide a clinician with information about the underlying cause of the sore throat and inform determination of the optimal treatment. This also highlights the importance of accurate laboratory tests in slowing increases in the prevalence of medication-resistant strains of disease bacteria.⁴⁷ While antibiotics have little to no effect on the cause of many upper respiratory infections (including all viral infections) whose symptoms often resemble those cause by GAS, U.S. clinicians often prescribe antibiotics for these infections.⁴⁸ As resistance to antibiotics commonly used to treat GAS has been documented,⁴⁹ accurate diagnosis of GAS using laboratory testing is a key component for preventing inappropriate use of antibiotics. Similarly, laboratories also conduct antimicrobial susceptibility testing to determine the ability of antimicrobial agents to inhibit the growth of pathogenic bacteria, thereby helping to optimize treatment and reduce the risk of antibiotic-resistant organisms.⁵⁰

Brain natriuretic peptide (BNP) is a peptide involved in the control of cardiovascular function; plasma concentrations of BNP are increased in individuals with heart failure and BNP levels are correlated with the severity of the symptoms.^{51,52} The BNP assay is used by clinicians to determine whether or not an individual has heart failure. For example, a 2004 study of patients presenting in the emergency department with acute dyspnea, or shortness of breath, found that, when used in conjunction with other clinical information, rapid measurement of BNP to diagnose heart failure improved patient evaluation and treatment and reduced the total time the patient spent in the emergency department.⁵¹ Study results indicated that 75% of patients in the BNP group were hospitalized, compared to 85% of the control group. Similarly, 15% in the BNP group required intensive care, compared to 24% in the control group.

Prognosis

Once a diagnosis is made and the severity of the disease has been determined, laboratory test results can contribute to projecting the course of disease, including estimating the likelihood that an individual will recover from a disease or medical condition. For instance, certain abnormal results in a panel of laboratory tests given to women who are suffering from severe pre-eclampsia are predictive of high risk of maternal morbidity.^{53,54} Routine laboratory tests ordered upon hospital admission of patients following myocardial infarction that measure white blood cell, creatinine, glucose, lactate dehydrogenase, and platelet counts are predictive of the likelihood of mortality.⁵⁵

Individuals who have had an unexplained thrombotic episode (i.e., clinical signs and symptoms associated with a blood clot in a vein or artery) before they are 50 years old or have had certain abnormal clots are encouraged to have a molecular diagnostic test to determine whether they have an inherited gene mutation that puts them at increased risk of developing additional blood clots.⁵⁶ The test detects factor V Leiden, a variant form of a factor V, a coagulation factor that is activated following injury of a blood vessel. Factor V Leiden is the most common inherited predisposition to abnormal clotting in the U.S. and individuals who are found to carry the mutation are counseled to avoid risk factors that can lead to additional blood clotting, such as oral contraceptive use.

Although not yet in routine practice, laboratory tests are increasingly used to determine the potential for future adverse health outcomes following recovery from a disease, such as recurrent stroke or cancer relapse. In February 2007, FDA cleared for marketing a test (MammaPrint®) that determines the likelihood of breast cancer returning within 5-10 years after a woman's initial cancer.⁵⁷ The test evaluates 70 genes located in the tumor to determine whether the patient is at low or high risk for spread of the cancer to another site. Like other predictive tests, the results from this and others being developed to assess likelihood of disease relapse are not perfectly accurate and must be used with other information to support management of the disease.⁵⁸ A similar laboratory developed test is the *Oncotype DX*TM that analyzes the expression of a panel of 21 genes to quantify the likelihood of breast cancer recurrence and potential benefit from chemotherapy in women with newly diagnosed, early stage invasive breast cancer.⁵⁹ Clinical practice guidelines of ASCO and NCCN include indications for using the *Oncotype DX*TM test, although these organizations await the findings of prospective clinical trials of this and other gene expression profile tests for offering more definitive guidance. Major U.S. payers cover the cost of the test for particular indications, sometimes subject to prior authorization.^{60, 61}

Monitoring General Treatment Effectiveness

Laboratory tests play a large role in monitoring and evaluating the efficacy of other medical treatments.⁶² They can assist clinicians in deciding whether to modify a specific course of treatment in order to optimize outcomes, including maximizing therapeutic impact. For instance, tests to measure viral load, CD4 count, complete blood count, and blood chemistry tests are commonly used to assess treatment response in patients with HIV.⁶³ Some laboratory tests used to monitor treatment effectiveness are the same as those used to make the initial disease diagnosis. A very common instance of this involves tests to measure thyrotropin/thyroid stimulating hormone in the diagnosis and monitoring of thyroid disease.⁶⁴ Laboratory testing is also important in monitoring patients following surgery to gauge the success and effectiveness of a procedure. Laboratory tests to detect levels of human chorionic gonadotropin in women with trophoblastic disease, which involves abnormal growth of cells inside a woman's uterus, are conducted regularly following surgery to determine whether or not further treatment is required.⁶⁵

Managing Acute Health Conditions

Acute conditions are those that appear suddenly and follow a short, severe course (i.e., persisting for several days or weeks) and have the potential to be completely resolved. Most acute care is relatively short-term. In acute care settings such as the intensive care unit (ICU) or the emergency department, frequent laboratory testing can be used to monitor quickly and accurately an individual's status and response to medical interventions. The five most commonly ordered

types of laboratory tests in ICUs include basic metabolic panels, arterial blood gas profiles, complete blood counts, partial thromboplastin times, and measures of magnesium levels.⁶⁶ The basic metabolic panel, which measures glucose, calcium, electrolytes, and analytes related to kidney function, is commonly ordered in hospital emergency rooms because its results can indicate several acute problems, including kidney failure, insulin shock or diabetic coma, respiratory distress, or heart rhythm changes.⁶⁷

Particularly in critical care settings, any intervention that shortens or improves the efficiency of care can dramatically affect patient outcomes and health care costs.⁶⁸ There is great emphasis on providing quick and accurate laboratory test results for individuals in critical care settings. One commonly used method of achieving short TATs is stat testing, which refers to the sequence of events to obtain urgently needed test results promptly.⁶⁹ Many hospitals maintain designated stat laboratory space to meet urgent testing needs, usually located next to operating rooms, critical care units, or the emergency department.⁷⁰ Recent research confirms that rapid analysis of cardiac markers D-dimer (a marker for patients at risk of a pulmonary embolism or deep vein thrombosis) and serum protein S100 (a marker of brain damage) improves outcomes.⁷¹⁻⁷³

Laboratory tests for certain critical conditions can be conducted using point-of-care testing (POCT) technology, which allows clinicians to obtain laboratory results in proximity to the patient.⁷⁴ Measurements of glucose and oxygen saturation levels at the point-of-care allows clinicians to determine changes in a patient's status rapidly and frequently.⁷⁵ In critical care settings, nurses often perform POCT.⁷⁰ Particularly in the emergency room, POCT has the potential to expedite decision making and allow for more effective triaging of patients.

While acute care is often provided in hospital settings (e.g., emergency department, ICU) it can also be provided in ambulatory care settings (e.g., physicians' offices, other primary care sites). As in critical care, laboratory testing in non-critical primary care is vital to timely and accurate diagnosis. For instance, testing for urine leukocyte esterase and nitrites to detect urinary tract infections, testing for *H pylori* to detect gastrointestinal disorders, and testing for C-reactive protein to detect bacterial infection are all commonly used in acute care provided in primary care settings.⁷⁶⁻⁷⁸ POCT is growing in use for non-critical acute care to provide rapid diagnosis and rule out other tests.⁷⁹ Whereas urine specimen culture testing requires 24 hours to complete, urine dip-stick tests provide a means of rapidly detecting the presence of bacteriuria and urinary tract infections.⁸⁰ Specimen culture and antimicrobial resistance susceptibility tests are usually conducted in a laboratory, while dipstick tests contain specially treated plastic strips that change color when exposed to infected urine and can be conducted in a doctor's office or at home. In many cases, negative urine dipstick tests alone can exclude the presence of infection.

Managing Chronic Health Conditions

Laboratory testing is an essential component in managing chronic diseases – health conditions that persist over an extended period of time and, in many cases, cannot be completely cured (e.g., type I diabetes).⁸¹ The burden of chronic disease in the U.S. population is high. More than 90 million Americans currently live with chronic illnesses. About half of older adults have at least two chronic medical conditions.⁸² Care for chronic illness accounts for more than three-fourths of U.S. health care costs.⁸³

Laboratory tests are useful tools for clinicians and patients in understanding the status of the disease(s), informing treatment decisions, determining the urgency of care required, managing symptoms, educating patients, and incorporating lifestyle changes into the treatment regimen. In certain instances, regular laboratory testing can prevent the diseases from progressing or worsening. For example, patients with coronary artery disease are at high risk for myocardial infarction. Aggressive lipid management in individuals who have heart disease helps to prevent heart attacks and reduces mortality rates.⁸⁴ Regular lipid testing of patients with heart disease helps physicians to tailor disease management regimens and provides a means to motivate some patients to implement lifestyle changes. Similarly, laboratory tests are a key component in the management of chronic kidney disease, which can also lead to high blood pressure, anemia, weak bones, nerve damage, and progression to kidney failure.⁸⁵ Laboratory tests that measure glomerular filtration rate are used to assess the severity of chronic kidney disease and to determine whether to initiate certain treatments.

Disease management refers to the ongoing care associated with chronic conditions. It is defined as a proactive, multi-component strategy for delivering health care services that aims to reduce adverse medical events by maximizing patient's adherence to prescribed treatments and/or lifestyle changes.⁸⁶ An important component of the strategy is self management, with patients being responsible for day-to-day self-monitoring, decision-making, and healthy lifestyle choices.^{87,88}

Diabetes treatment has been used often as the focus of models for disease management, which traditionally involves a partnership between physicians, nurses, educators, and the patient. Physicians monitor patient blood glucose and HbA1c levels during regular office visits and track trends over the previous two-to-three months. Frequent, daily self-monitoring of blood glucose levels also is critically important to determine medication and/or dietary changes needed.⁴⁵ Individuals usually self monitor by using a lancet device to obtain a small blood sample that is then applied to a reagent strip and inserted into a reflectance photometer for an automated reading of blood glucose levels.⁸⁹ Patient education is needed for successful disease management at home.⁹⁰ Newer technologies support continuous glucose monitoring by measuring interstitial fluid using minimally invasive methods or by applying noninvasive electromagnetic radiation through the skin to the body's blood vessels.⁹¹ Continuous monitoring provides clinicians and patients with greater insight into glucose levels throughout the day than does conventional self-monitoring, thereby helping to identify and ultimately prevent periods of hypo- and hyperglycemia.

Therapeutic Drug Monitoring

Standard laboratory tests are integral to the management of medication dosages for many conditions. Therapeutic drug monitoring (TDM) refers to the measurement of specific drugs or metabolites in the body via blood testing to inform therapeutic regimens that maintain a target medication concentration in the body.⁹² Maintaining an appropriate dosage is particularly important for medications with a narrow therapeutic index, i.e., drugs with smaller dosage ranges for optimum effectiveness. Medications with narrow therapeutic indexes, such as those used to treat cardiovascular, kidney, thyroid, and liver disease, typically require precise dosage modifications to fit the needs of an individual patient as well as close monitoring. Drugs that have a wider therapeutic index, such as antihypertensives and antibiotics, can usually be prescribed based on pre-established dosing schedules.

Laboratory tests associated with TDM are instrumental in establishing and maintaining the medication dosage that will yield the optimum blood level range for a specific individual.⁹² Calculations are based on optimum therapeutic ranges developed through research and clinical testing of narrow therapeutic index medications in addition to individual patient testing. TDM plays an especially vital role in ensuring that treatments are fully effective and that the individual does not experience any toxicity as a result of treatment. TDM can also be used to evaluate the extent to which an individual is compliant with or adherent to a clinician's prescribed course of treatment.

Most TDM takes place in hospitals or other inpatient settings; however, newer tests are allowing TDM to be conducted in other settings, such as clinics, physicians' offices, and at home.⁹³ Certain medications, such as warfarin, also can be monitored at home between physician's visits with portable monitoring devices similar to those used by diabetics to monitor glucose.⁹⁴ TDM conducted on-site in physicians' offices has the benefit of enabling clinicians to adjust therapeutic drug doses while the patient is still present in the office.⁹⁵ On-site analyzers enabling TDM in physicians' office laboratories (POLs) are available for measuring concentrations of anticonvulsant and anti-asthmatic medications, among others. POCT available for POL-based TDM allows clinicians to obtain laboratory results more quickly and cost-effectively than when specimens are sent to a laboratory. Immunosensor applications that use antibodies to detect drug concentrations can be plugged into handheld personal digital assistants to allow clinicians to obtain TDM results in 30 minutes or less in both hospital and outpatient settings.⁹⁶

Detection and Prevention of Medication Error

Laboratory testing also provides a means to prevent and detect medication errors,^b i.e., any error occurring in the medication-use process, such as wrong dosages prescribed, wrong dosage administered, failure to administer a medication by the provider, or patient failure to take the medication as prescribed.¹⁰⁰ Computerized physician/practitioner order entry systems, which allow users to order medications electronically, can compare the medication orders to major elements of the patient's history, including laboratory results. Clinicians are alerted when medication orders conflict with a specific element in the patient's history.¹⁰¹ Increased networking of computerized ordering systems, pharmacy information systems, and laboratory information systems should further increase the ability of laboratory medicine to aid in the prevention of medication errors. Review of laboratory test results documented in a patient's medical record aids in the detection and identification of medication errors.^{100, 102}

^b An *adverse drug reaction* (ADR) is any adverse effect resulting from the use of a medication in the recommended manner. An *adverse drug event* is any injury due to medical harm, including physical harm (e.g., rash), mental harm (e.g., confusion), or loss of function (e.g., inability to drive a car), whether used in the recommended manner or not. ADRs and events may be preventable or nonpreventable. A *medication error* is any error occurring throughout the medication-use process, including events resulting from use of a medication in both recommended and non-recommended manners. An error is the failure of a planned action to be completed (i.e., error of execution), or the use of a wrong plan to achieve an aim (i.e., error of planning), and may be an act of commission or omission.⁹⁷⁻⁹⁹

Individualizing Drug Treatments and Reducing Adverse Drug Reactions

As scientists study the human genome and gain understanding of the genetic, behavioral, and environmental determinants of disease and therapeutic response, laboratory tests can be leveraged to individualize treatment protocols based on individual patient traits. Pharmacogenomics (PGx)^c uses information from the human genome to understand the spectrum of genes involved in drug response and studies the relationship between gene-based markers and pharmacology.^{104,105} By assessing factors such as hormone levels and gene expressions that can vary among individuals, PGx allows clinicians to better understand how an individual is likely to respond to a specific treatment or therapy and, thereby, to tailor treatment most appropriately. PGx is a key element of the broader concept of personalized health care.

Molecular laboratory tests provide information used to apply PGx. Tests for estrogen and progesterone receptors on the surface of cells from tissue biopsies of women with breast cancer can determine whether the growth of these cancers can be stopped by therapeutic molecules that block these hormones.¹⁰⁶ Trastuzumab (Herceptin), a monoclonal antibody used in the treatment of breast cancer, is considered to be effective only in women whose breast cells express the HER2/neu protein, the presence of which is determined by laboratory tests.¹⁰⁷ The efficacy of certain drugs for treating HIV infection is mediated by specific genetic polymorphisms; individuals expressing a single-nucleotide polymorphism on the *MDR1* gene respond more favorably to anti-retroviral agents.¹⁰⁸ Response to warfarin, a commonly prescribed drug for individuals at high risk of developing blood clots, varies; individuals with the *2 and *3 allelic variants of the cytochrome P450 2C9 enzyme clear the drug much slower than individuals without this allelic variation, and therefore require lower doses.^{109,110} A major goal of determining optimal warfarin dosage is to reduce adverse reactions and to determine the optimal therapeutic dosage.

PGx testing can also be used to identify individuals who are at risk for developing an adverse drug reaction.⁹⁷ When therapeutic drugs are indicated, PGx testing can improve appropriate drug selection and management of medication dosage, as well as reduce the potential for adverse drug reactions (ADRs).^{111,112}

Several PGx tests are readily available for preventing ADRs. One example is laboratory testing using DNA microarray assays to identify variants in cytochrome P450, a group of drug-metabolizing enzymes that exists in more than 50 forms and catalyzes the oxidation of many drugs, including beta blockers, antiarrhythmics, and antidepressants.^{d,114,115} Similarly, administration of 5-fluorouracil, a chemotherapy used in the treatment of various types of cancer, can lead to potentially life-threatening toxicity in individuals with dihydropyrimidine dehydrogenase deficiency.¹¹⁶ Laboratory testing can be used to identify individuals with a defect in the gene that encodes for the dihydropyrimidine dehydrogenase deficiency enzyme, thereby allowing clinicians to make more appropriate treatment decisions.

^c Pharmacogenomics is defined as the general study of all of the genes that influence and determine drug behavior.

The term *pharmacogenetics* refers to the study of particular inherited differences in drug metabolism and response. However, the two terms are used interchangeably, and this distinction is considered arbitrary.¹⁰³

^d Research into targeted drug treatments is promising. For instance, a 2007 systematic review prepared on behalf of CDC's Evaluation of Genomic Applications in Practice and Prevention Project determined that there is a paucity of good-quality data addressing whether testing for *CYP450* polymorphisms in adults who are about to enter treatment for non-psychotic depression leads to improved outcomes.¹¹³

Because PGx makes feasible developing laboratory tests capable of identifying patients and conditions that will be responsive to highly targeted therapeutic agents, clinical laboratories are expected to play a greater role in the development of this field over the next several years.¹¹⁷ In particular, clinical laboratories are expected to provide consumers with access to PGx testing and to provide clinicians with the evidence required to make decisions regarding medical applications.¹¹⁸ As knowledge builds about the utility of genetic information for tailoring drug therapies, the number of PGx tests is expected to increase. In order for PGx to make a significant contribution to personalized health care and have an impact on population health, many more molecular biology tests than are currently available to detect genetic polymorphisms will have to be validated.^{119, 120} Laboratories will have important roles in studies to identify and verify polymorphisms and clinical trials of PGx-guided interventions.

PROTECTING THE BLOOD SUPPLY AND TRANSPLANT RECIPIENTS

Blood and blood products are vital health care resources that are required in a large number of medical procedures. Availability of safe blood and blood products is essential for millions of people in the U.S., including accident victims, transplant recipients, and patients undergoing a wide range of surgeries.¹²¹ The health care industry relies on blood donations from volunteers in order to meet this demand. In 2001, the most recent year for which data are available, U.S. institutions collected more than 15 million units of whole blood and red blood cells, approximately 14 million units of which were transfused to 4.9 million patients.¹²²

Through their blood banking responsibilities, clinical laboratories work to guarantee the safety of the blood supply. Blood collection usually takes place at community blood centers, hospital-based donor centers, or mobile sites temporarily constructed for blood donations.¹²² Following donation, the blood is taken to blood banking laboratories and tested to determine blood type and detect the presence of antibodies, bacterial contamination, and other agents that could potentially cause adverse reactions in transfusion recipients. Once testing is completed, donated blood that is free of infection is stored for future use.^e

Screening blood donations for the presence of infectious disease is a high-value service provided by blood banks and clinical laboratories. Laboratories screen donations for the presence of HIV and hepatitis B and C viruses, the three transfusion-transmitted viruses of greatest concern to public health.¹²³ Blood donations have been tested for the presence of HIV-1 infection (the strain of HIV found most commonly in the U.S.) since 1985.¹²⁴ Until 1999, testing for HIV-1 required that the donor's immune system had already mounted a response against the virus, allowing for a "window period" in which HIV-contaminated blood would be undetected by laboratory testing for HIV antigens and antibodies. The creation and implementation of nucleic acid testing (NAT) in 1999 under an FDA-approved Investigational New Drug application (followed by FDA approval of a commercial assay in 2002) reduced this window period by almost half, from an average of 22 days to 12 days. Relative to antibody and antigen tests, which reduced the risk of HIV infection from a single blood transfusion to approximately 1 in 676,000, NAT reduces the risk

^e Storage methods are determined by the component of blood being stored and how quickly the donation will be used. Red blood cells can be refrigerated for a maximum of 42 days or frozen for up to 10 years; platelets can be stored at room temperature for up to 5 days; and fresh frozen plasma can be frozen for up to 1 year.¹²²

of transfusion-transmitted HIV-1 to about 1 in 1.9 million blood units.^{125, 126} Innovations in laboratory testing have also allowed donated blood to be screened for human T-lymphotropic virus types I and II, syphilis, West Nile virus, Chagas' disease, and other infections.¹²²

Clinical laboratories also conduct blood compatibility testing, or hemocompatibility, to determine whether a particular unit of blood can be safely transfused into an individual.¹²⁷ Pretransfusion hemocompatibility testing includes identifying an individual's ABO blood group and Rh type, both of which are determined by the presence or absence of specific antigens on red blood cells, as well as testing blood for unexpected red cell antibodies.¹²² Cross-matching determines whether an individual's blood has antibodies that will react with the donor's cells. In the event that a cross-match indicates a reaction, laboratory professionals identify the specific reacting antibodies and locate alternate donor blood that lacks the antigen.

Compatibility testing, cross-matching, and other precautions taken by clinical laboratories help prevent adverse transfusion outcomes, which include acute hemolytic transfusion reactions, febrile nonhemolytic transfusion reactions, allergic reactions, volume overload, and acute lung injury caused by transfusing incompatible blood.¹²⁸ ABO incompatibility is the most common cause of acute hemolytic transfusion reactions, which usually result from antibodies in the recipient's plasma reacting to red blood cell antigens in the donor blood. Technologies such as portable data terminals that scan patient wristbands at the bedside, bar-coded specimen labels, and electronic transfer of test results to the laboratory can decrease the risk of a mismatch between blood recipients and donor blood caused by misidentification and are increasingly the focus of laboratories, hospitals, and accreditation bodies in the U.S.^{129, 130}

DETECTING EXPOSURE TO ILLEGAL OR TOXIC DRUGS

Exposure to illegal drugs, toxic substances, and incorrect use of therapeutic drugs are major causes of hospital emergency department visits in the U.S. In 2004, the most recent year for which data are available, an estimated 1.08 million visits to the emergency department were attributed to poisoning and toxic effects, representing approximately 1% of all visits.¹³¹ As many as 23% of emergency department visits each year may be attributed to the abuse of alcohol and other substances.¹³² In addition to alcohol and drugs of abuse, accidental or inadvertent contact with substances such as organophosphorous compounds (used in pesticides), rodenticides, heavy metals, and carbon monoxide can also contribute to significant acute and chronic threats to health.¹³³

Rapid, accurate laboratory testing enables clinicians to identify specific toxic substances to which individuals have been exposed and to determine appropriate medical care, including what medications can be prescribed and how quickly treatment must be initiated.¹³⁴ Toxicology screenings, most often performed on blood or urine samples and sometimes on gastric contents, allow clinicians to evaluate the type and approximate amount of legal and illegal drugs an individual has consumed.¹³⁵

In its 2005 guideline, the National Academy of Clinical Biochemistry (NACB) divides toxicology screening into two tiers:

- Tier I testing includes stat testing for selected agents in serum, plasma, and urine.

- Tier II testing is for individuals who have been admitted to the hospital who remain intoxicated or comatose and for whom tier I testing did not identify the nature of the problem.¹³⁴

NACB recommends that hospital emergency departments conduct serum toxicology assays to detect 14 different substances, including lithium, salicylate, valproic acid, digoxin, methyl alcohol, and iron, and urine toxicology screenings to detect seven substances, including cocaine, barbiturates, and opiates.

Due to the nature of acute illness and poisoning and limitations in resources and technology, clinical laboratories are limited in their ability to provide real-time analyses of a full spectrum of toxicological screens for patients who appear to be impaired or overdosed. This highlights the importance of TAT for laboratory tests ordered in the emergency department. For a few tests, rapid bedside toxicological screening assays allow clinicians to obtain laboratory test results in real time at the point-of-care. Many emergency departments use breath meters for determining alcohol concentrations in intoxicated patients at the bedside; these are accurate, precise, and relatively inexpensive.¹³⁴ Point-of-care immunoassays are also available for a wide variety of drugs of abuse, including cocaine, methamphetamine, and antidepressants.¹³⁶ However, many rapid toxicological screening tests have not yet been validated in the emergency department setting.¹³⁷ Specifically, rapid assays for methanol and ethylene glycol poisoning, which can produce significant morbidity and mortality, are being tested currently but are not yet in wide use.¹³⁸

In 2002, 4 million adults in the U.S. diagnosed with serious mental illness also had a substance abuse disorder.¹³⁹ Because substance abuse can exacerbate psychiatric symptoms, toxicology screening is especially important in the emergency treatment of serious mental illness.¹⁴⁰ Clinicians are often asked to perform laboratory testing on individuals presenting with acute behavioral emergencies in order to rule out illnesses that may be causing acute psychiatric symptoms. The results of laboratory testing, particularly toxicology screening, can identify substance abusers and help guide treatment of psychiatric patients.

VALUE TO THE MEASUREMENT OF QUALITY OF CARE

The IOM defines quality of care as “the degree to which health care services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.”¹⁴¹ Health care quality measures enable health care decision-makers to compare quality of specific aspects of health care to relevant reference standards or criteria. They are increasingly used to measure and assess the performance of the U.S. health care system.¹⁴² Quality can be measured in three main dimensions:

- *Structure* refers to the environmental factors that support the capacity to achieve quality
- *Process* refers to what is done to and for the patient
- *Outcomes* refers to changes in patients’ health status as a result of care received¹⁴³

Most health care quality literature focuses on process of care measures, examining the appropriateness of the care provided and the adherence of providers to professional standards.¹⁴⁴

Laboratories monitor quality in order to ensure that they are providing information that is timely, accurate, appropriate, and interpretable, and ensures high quality care.¹⁴⁵ Quality indicators within laboratory medicine can also be classified under structure (e.g., staffing benchmarks of productivity, policies for documenting safe phlebotomy practices), process (e.g., patient identification errors, analytic accuracy, follow up with clinicians regarding results), or outcomes (e.g., health outcomes, customer satisfaction, cost-effectiveness).^{7, 146, 147}

Quality Measurement for Priority Health Conditions

Data derived from laboratory testing is a key component in many of the current quality measures, particularly those that assess health outcomes, the quality measures most relevant to consumers and many health care plan purchasers.^{148, 149} Laboratory-based performance is assessed with process and outcome measures developed for such highly prevalent and/or burdensome conditions as diabetes, heart failure, ischemic heart disease, stroke, end-stage renal disease, pneumonia, cervical and colon cancer, and pregnancy and childbirth.⁷ For instance, the American Quality Alliance explicitly includes the use of laboratory tests to measure HbA1c and low density lipoprotein cholesterol as a performance measure to assess the quality of diabetes care.¹⁵⁰

Two national sources of validated quality measures include the Health Plan Employer Data and Information Set (HEDIS), maintained by the National Committee for Quality Assurance (NCQA) and the National Quality Measures Clearinghouse (NQMC), maintained by AHRQ.^{151, 152} HEDIS data can be used by purchasers and patients to make side-by-side comparisons of health care plans and by health plans to evaluate their own performance. Approximately 90% of managed care organizations use HEDIS measures to assess provider performance. CMS also requires plans participating in Medicare programs to report on HEDIS measures.¹⁵³ The NQMC database provides information on evidence-based health care quality measures linked to a particular disease or condition and a particular treatment or intervention. The information can be used by practitioners, providers, payers, and purchasers to inform health care decisions. A search of the HEDIS and NQMC reported in 2005 found that 23% of HEDIS measures and 14% of NQMC measures used to assess the quality of care given by a specific provider or health plan are direct measures of laboratory test use for measuring health risks, diseases, or medical conditions.¹⁵⁴

Performance measurement, including in laboratory testing, can have a direct impact on delivery, quality, and cost of health care and on the establishment of best practices. According to NCQA, in 2005, more than 70 million Americans benefited from health care improvements facilitated by quality measurement. Individuals enrolled in health plans that use and publicly report performance data are more likely to have received preventive care and care for chronic conditions in accordance with evidence-based clinical guidelines.¹⁵⁵ Under-compliance with HEDIS measures is associated with an increase in the number of avoidable deaths and avoidable hospital costs. For instance, failure to conduct regular HbA1c testing resulted in an estimated 7,400-15,000 avoidable diabetes-related deaths and \$1.35-1.62 billion in avoidable hospital costs in 2005, according to NCQA.¹⁵⁵

Indicators of Quality of Laboratory Processes

Performance measurement is a valuable tool that can improve testing processes, benchmark progress, and standardize laboratory performance. It also has the potential to decrease waste and inefficiencies in the laboratory and lead to better health outcomes.¹⁵⁶

To date, performance measurement in laboratory medicine has focused mostly on the analytic processes (i.e., the actual testing of specimens) in order to meet regulatory requirements of the CLIA. More specifically, regulatory agencies and accrediting organizations have impelled quality control and quality assurance initiatives during the last 15 years, mainly in the form of proficiency testing, a quality monitoring approach for evaluating laboratories' performance of selected tests and their ability to arrive at the "correct" result.¹⁴⁵ Other facets of laboratory performance associated with the preanalytic and postanalytic phases also are evaluated, such as test turnaround time and specimen identification errors. As a result of these requirements, the quality and safety of laboratory testing has improved significantly over the past 20 years.^{157, 158}

Historically, quality measures for preanalytic and postanalytic phases of the testing process have received less attention, although some accreditation organizations and laboratories have taken the initiative to assess quality and errors in these areas.^{159, 160} The quality assurance measures employed by The Joint Commission, CAP, AABB, and COLA, have targeted certain elements of preanalytic and postanalytic processes including methods to improve patient identification, specimen collection, test turnaround time, notification of critical values, and customer satisfaction.^{161, 162}

Outside the context of proficiency testing, formalized performance measurement and public reporting on key quality indicators in a manner reflecting the broader health system (e.g., HEDIS measures) has not yet been instituted in the laboratory medicine sector. However, CDC, CMS, other government agencies, accreditation organizations, and stakeholders have been collaborating to develop a set of such measures for national reporting and the determination of best practices.^{7, 163} Studies and programs undertaken by accreditation organizations, academic researchers, and government agencies will provide an evidence-based foundation for more comprehensive quality measurement. CDC announced a funding opportunity in 2007 to evaluate clinical laboratory practice by identifying evidence-based laboratory medicine practices, particularly those associated with the pre- and postanalytic stages of the total testing process.¹⁶⁰ While the quality of laboratory testing is already high, implementing a comprehensive standardized performance measurement program will add further value to the overall health system and quality of patient care.

Value-based Purchasing and Pay-for-Performance

Value-based purchasing is among the evolving mechanisms being applied in various sectors of health care to address rapidly rising health care costs and concerns about shortfalls in quality. It refers to arrangements in which buyers hold health care providers accountable for cost and quality, and includes the following attributes:

- Contracts that specify the responsibilities of employers as purchasers and insurance, managed care, and hospital and physician groups as suppliers
- Incentives that reward specific practices by providers and consumers
- Information that supports purchasing activity management
- Quality management that leads to continuous improvements in the health care purchasing process and in the delivery of health care
- Education that helps employees to become better consumers of health care¹⁶⁴

Pay-for performance (“P4P”), a reimbursement arrangement in which a portion of provider payments are tied to performance measures associated with quality of care, has been proposed as one means of enabling value-based purchases.^{165,166} By 2005, there were more than 150 P4P programs and initiatives in the U.S., sponsored by various health care plans, employers, and government purchasers.^{147,167} Approximately 80% of P4P programs are sponsored by private health plans, but some are sponsored by government payers, including Medicare and state Medicaid programs.¹⁴⁷ Primary care physicians are the main target of P4P initiatives while 60% of programs involve specialists and 20% involve hospitals.

Expert testimony to Congress on the subject of value-based purchasing of physicians’ services has routinely cited variation in laboratory testing and physicians’ use of laboratory testing as a way to measure the efficiency and quality of care being provided.¹⁶⁸⁻¹⁷⁰ For example, laboratory testing provides clinicians with objective means for improving performance, such as ordering appropriate follow-up testing for patients with test results indicating out-of-range or otherwise abnormal values.¹⁷¹ In turn, data that include laboratory testing can be used by consumers and purchasers to assess the quality of health care provided by different clinicians or organizations. Laboratory-related professional organizations, such as the College of American Pathologists (CAP), are partners in the development of P4P measures. CAP led development of P4P pathology-related measures for breast and colon cancer, which were approved by the American Medical Association (AMA) in June 2007.¹⁷²

Still, P4P represents a relatively new type of financing mechanism for the health care system, and its evidence base is small. A 2006 systematic review of the published literature examining P4P programs for the period 1980-2005 identified only 17 empirical studies of explicit financial incentives for quality, and could conclude little about the impact of these arrangements.¹⁷³ No studies examined the optimal duration of financial incentives for quality or the persistence of their effects after termination, and only one study addressed cost-effectiveness. The investigators called for ongoing monitoring of the impact of current programs and further research to guide implementation of financial incentives and to assess their cost-effectiveness.

VALUE TO PUBLIC HEALTH AND SURVEILLANCE

Public health surveillance refers to ongoing, systematic collection, analysis, and interpretation of data related to health that is vital to the planning, implementation, and evaluation of public health practice. It relies on facets of clinical and public health laboratory testing.¹⁷⁴ Services provided by clinical laboratories help to identify the nature of public health threats at both the individual and population level, including infections acquired during care, development of drug resistance, infectious disease outbreaks, and biological threats.

Health Care Associated Infections

Health care associated infections (also known as nosocomial infections) are those that develop in hospitalized patients in the absence of evidence that the infections were present or incubating at the time of admission.¹⁷⁵ The greatest common risk faced by hospitalized patients is health care associated infection, a major source of morbidity and mortality in the U.S. Up to 2 million patients experience a health care associated infection every year, and approximately 88,000 people die annually as a result of these infections.¹⁷⁶ Monitoring health care associated infection rates

and understanding their causes are necessary for hospitals to reduce the incidence of these infections and their impact on health outcomes and costs.

Microbiology laboratories help hospitals to monitor and control health care associated infection rates at individual and population levels. They are responsible for providing easy access to high-quality, timely data and support for epidemiological analyses.¹⁷⁵ Activities may include providing training on basic microbiology to hospital infection control program staff, monitoring laboratory results for unusual findings (e.g., clusters of pathogens indicating an outbreak, emergence of multi-drug-resistant organisms), strain typing of results, and storing specimens for further study.

Hospital laboratories with infection control practitioners voluntarily report health care associated infection rates to CDC. The National Nosocomial Infections Surveillance (NNIS) system^f was established by CDC in the 1970s to monitor the incidence of health care associated infections in the U.S. and to assist infection control professionals in managing endemic and epidemic health care associated infection outbreaks.¹⁷⁸ NNIS has contributed to significant reductions in bloodstream infection rates in coronary, medical, pediatric, and surgical ICUs.¹⁷⁹ More than 300 hospitals participate in the NNIS; microbiology laboratories at each of these hospitals provide the NNIS with information related to health care associated infection rates.¹⁷⁸ The system has been updated and expanded into the National Healthcare Safety Network, a web-based surveillance system that was launched by CDC's Division of Healthcare Quality Promotion in 2005. The National Healthcare Safety Network aims to improve patient and health care worker safety by monitoring adverse events associated with devices, procedures, and medications, providing comparative data for performance improvement, and ensuring access to prevention tools and information about lessons learned and best practices.¹⁷⁷

Multi-drug-resistant Organisms

Another common problem faced by health care facilities is multi-drug-resistant organisms (MDROs). MDROs are microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents. They are difficult to treat and can result in increased length of hospital stay, higher cost, and greater chance of mortality in infected individuals.¹⁸⁰⁻¹⁸³ MDROs are often the cause of health care associated infections. Health care facilities at particular risk for MDRO outbreaks include those caring for older patients, acute care settings, and ICUs.¹⁸⁴ Varying temporally, geographically, and by health care setting, the prevalence of MDROs in the U.S. has increased steadily in recent decades. While only 20-25% of *Staphylococcus aureus* was resistant to methicillin and other antibiotics in the early 1990s, resistance rose to 59% by 2003.^{185, 186}

Clinical laboratories monitor MDROs at the levels of patients, institutions, and populations. At the level of individual patients, laboratories conduct antimicrobial susceptibility testing, which involves isolating and testing pathogenic bacteria to determine the ability of antimicrobial agents to inhibit their growth.⁵⁰ The results of susceptibility testing help guide clinician decisions about how to treat specific infections. Many of the roles played by microbiology laboratories with regard to health care associated infection surveillance and education also apply to MDROs.¹⁷⁵ In

^f The NNIS, with the National Surveillance System for Health Care Workers and the Dialysis Surveillance Network, is undertaking a major redesign to become the National Healthcare Safety Network, which will cover new areas of patient safety monitoring and evaluation.¹⁷⁷

2000, the CAP Microbiology Surveys Program assessed the frequency and accuracy of susceptibility testing at 3,857 microbiology laboratories in the U.S. CAP found that laboratories generally demonstrated acceptable test accuracy and reproducibility for the most commonly used antimicrobial susceptibility testing systems or methods.¹⁸⁷

Laboratories support national monitoring of MDROs. The National Antimicrobial Resistance Monitoring System for Enteric Bacteria is part of CDC's Emerging Infections Program's Epidemiology and Laboratory Capacity Program and the Foodborne Diseases Active Surveillance Network.¹⁸⁸ In 2004, the most recent year for which data are available, public health laboratories from all 50 states sent isolates to CDC laboratories for antimicrobial susceptibility testing.¹⁸⁹ CDC's Epidemiology and Laboratory Capacity for Infectious Diseases program, part of the National Center for Infectious Diseases, has cooperative agreements with state and local public health agencies in all 50 states to identify, characterize, and respond to infectious diseases, including MDROs.¹⁹⁰

Public Health Reporting of Adverse Events

Laboratories participate in the reporting of adverse events related to testing technologies and abnormal test results that result in patient harm. FDA's MedWatch program gathers data on all marketed medical products submitted by clinicians, manufacturers, and consumers and includes adverse event reporting for laboratory test failures that result in harm to a patient. The Joint Commission's (formerly known as the Joint Commission on Accreditation of Healthcare Organizations) Sentinel Event database collects data on unexpected occurrences involving serious physical or psychological injury or risk thereof; laboratories accredited by the Joint Commission are required to submit reports to the database.¹⁹¹ The Joint Commission publishes Sentinel Event Alerts for its accredited organizations that identify specific events and their underlying causes and suggests ways to prevent such occurrences in the future.

Natural Disasters and Biological and Chemical Threats

Laboratories assist in meeting the challenges of natural disasters and biological and chemical events. Several national programs aim to provide a mechanism for communication between laboratories and a means to link public and private laboratories. Some of these initiatives include the following:

- The **National Laboratory System** is an initiative founded by CDC to improve cooperation and coordination among all public and private U.S. laboratories. Development of this system is still underway.¹⁹² The goal of the National Laboratory System is to promote public health laboratory leadership by improving the overall quality of laboratory testing and communication between public health and private clinical laboratories.
- The **Public Health Information Network (PHIN)** is a CDC initiative to promote national advancement of fully interoperable information systems in organizations that participate in public health and public health preparedness.¹⁹³ The goal of PHIN is to ensure that public health programs have near real-time access to data during acts of terrorism or disease outbreaks by developing, promoting, and using industry standards for data and technology.¹⁹⁴ In 2005, PHIN described functional requirements and general workflow for information systems responsible for managing laboratory testing.¹⁹⁵ The interoperability requirements include such basic functions as assignment of

unambiguous identifiers to laboratory data, adherence to PHIN standards for message exchange systems, and vocabulary standards. The Laboratory Response Network Results Manager supports the functional requirements established by PHIN.¹⁹³

- The **Early Warning Infectious Disease Surveillance (EWIDS)** was created in 2003 and is funded by DHHS.¹⁹⁶ EWIDS comprises state, federal, and international partners working together to ensure rapid, effective laboratory confirmation of infectious disease reports in the border regions of the U.S., Canada, and Mexico. Ongoing EWIDS projects include the development of cross-border surveillance protocols, a database directory of laboratories, and a Health Alert Network and cross-border secure internet information exchange. In 2006, DHHS announced a \$5 million contract to assist the six Mexican states in creating EWIDS systems at the U.S.-Mexico border that are coordinated and interoperable with currently existing EWIDS systems in the U.S.¹⁹⁷
- The **Laboratory Response Network** was established by CDC in 1999 as a network of laboratories capable of quickly responding to biological and chemical terrorism and other threats to public health.¹⁹⁸ It includes approximately 150 laboratories responsible for biological response. National laboratories located at CDC and the U.S. Army Medical Research Institute for Infectious Diseases in Maryland are the national laboratories that perform confirmatory testing for disease agents.¹⁹⁹ Reference laboratories, such as those run by state and local public health departments, perform confirmatory tests for biological agents, allowing local authorities to respond more quickly to positive test results. Sentinel laboratories are private, commercial, and hospital-based and test patient specimens as part of their daily testing regimen, allowing them to identify unusual results and refer suspicious specimens to the network's reference laboratories. This network provides a chain-of-command for reporting laboratory results and sharing laboratory data.

Another laboratory role in public health surveillance is response to biological or chemical terrorism. In cases of an overt biological or chemical threat, law enforcement officials are usually notified first, followed by notification of the Federal Bureau of Investigation, state emergency management, and state or local public health officials.¹⁹⁹ These agencies, in turn, are to contact CDC for a joint assessment of the validity of the threat. In the event of a valid threat, state or local public health laboratories that are part of the Laboratory Response Network are to test samples of the suspicious substance. Laboratory staff can identify the unknown substance and perform confirmatory testing to validate test results.

Laboratories are involved in mitigating adverse outcomes during natural disasters. Laboratories diagnose and confirm the presence of communicable diseases and ensure that basic laboratory tests are available to use in caring for injured individuals.²⁰⁰ Increasingly, POCT is being used to enable faster and more accurate diagnosis, triage, and patient monitoring during disasters. POCT was especially vital in the aftermath of Hurricane Katrina in August 2005.²⁰¹ The hurricane resulted in temporary closing of 12 hospitals (and their laboratories), local trauma centers, and an independent laboratory. POCT devices already on site, including glucose meters, whole-blood analyzers, and tests for infectious diseases, pregnancy, and prothrombin time, were used to provide care to thousands of affected people. Public health laboratories in states not affected by the hurricane assisted Louisiana and Mississippi public health laboratories, providing such services as newborn screening and water safety tests.²⁰²

QUANTIFYING VALUE USING COST-EFFECTIVENESS ANALYSIS

Analyses of the tradeoffs of the costs and benefits of health care are of increasing interest, particularly in instances where interventions offering marginal improvements over standard care are accompanied by large price increments.²⁰³ At present, coverage policies of Medicare and most commercial payers is based entirely or largely on clinical evidence rather than on cost-effectiveness or any other economic-related assessment.²⁰⁴ However, more commercial payers, hospitals and other health care institutions, and policy makers are seeking information from manufacturers and vendors of health care technologies, including laboratory tests, regarding whether their new and existing technologies are cost-saving, and sometimes more cost-effective, than alternatives. Interest in economic analyses that can inform these decisions appears to be growing among health plans and public and private sector payers. Health plans are using this type of information to develop drug formularies and tiered co-payment systems. At certain points throughout its history, CMS has proposed using, though has not employed, cost-effectiveness as an explicit criterion for determining coverage of new medical technologies.²⁰⁵ FDA performs cost analyses in certain instances, particularly to fulfill requirements for assessment of the economic impact of regulations; but the agency does not perform such analyses to inform market approval or clearance decisions for particular products.²⁰⁶ A survey conducted in 2001 of medical directors of 228 managed care plans found that 90% of plans considered cost in some regard when evaluating new medical intervention; however, only 40% reported using formal economic analyses for these purposes.²⁰⁷

Cost-effectiveness analysis (CEA) is one main type of economic analysis that is used to evaluate and compare the economic impact of health technologies and medical procedures. It quantifies the incremental (marginal) cost per incremental unit of effectiveness achieved with a technology versus the standard of care. Units of effectiveness are typically “natural” health units, such as case of cancer detected or life-year saved. Costs accrue differently to various stakeholders; depending on its purpose, a CEA can be conducted from the perspective of, e.g., the health care provider, payer/health plan, or society-at-large.

Another unit used in CEA is the quality-adjusted life year (QALY). QALYs are units comprising quality of life (assessed as patient utility for a given health state, ranging from 0.0 for death to 1.0 for perfect health) and length of life, and, thus, are not confined to use for particular diseases or conditions.²⁰⁸ (CEAs that assess tradeoffs between costs and some measure of patient utility for a health state or outcome are also known as cost-utility analyses.) Though used more in other industrialized countries, cost per QALY is used informally as a means to gauge value-for-money by some commercial U.S. health plans, though not by Medicare.^{205, 209-211} Though no formal threshold is used by U.S. payers, there is informal recognition that incremental cost-effectiveness ratios (ICERs) of up to \$50,000-\$100,000 per QALY are of acceptable value. It is also recognized that the ratios for many technologies in mainstream care exceed that magnitude.²¹² (In the U.K., technologies with ICERs approaching £30,000 per QALY tend to draw greater scrutiny by the National Health Service, although there is no formal cut-off level for inclusion as a health care benefit in that system.²¹³) Even though a laboratory test may result in a clinically significant improvement in health outcomes (e.g., via an informed treatment decision and course of care), doing so at a high cost may decrease payers’ willingness to cover it or to pay a premium price for it.

CEA of Genetics and Pharmacogenomic Tests

Among laboratory testing services, the potential economic impacts of genetic and PGx testing are gaining greater scrutiny. Even so, the number and quality of available CEAs remain limited. A small number⁸ of systematic reviews of economic evaluations of genetic testing (not including PGx) have been published in recent years.

Most of the economic evaluations of genetic testing found in the literature are CEAs, with relatively few cost-utility analyses and cost-benefit analyses. One review counted 37 CEAs, 16 cost-utility analyses, 12 cost-benefit analyses, and 4 cost-minimization analyses published between 1990 and 2004. Another review counted 47 CEA, 13 cost-benefit analyses, 7 cost-utility analyses, and 22 “other” economic evaluations published between 1983 and 2005.^{217, 218} These systematic reviews are limited because they excluded all disease-specific studies that did not explicitly refer to “genetics.” For example, at least 14 economic evaluations of screening for hereditary hemochromatosis (an inherited disorder that increases the amount of iron absorbed from the gut) were excluded in these four reviews.

In one of the systematic reviews of economic analyses for genetic testing published during 1990 through 2004, outcomes assessed in a majority of the studies were life-years gained or, simply, cases detected. QALYs were used in another 25% of the studies. Nearly 40% of the studies addressed cancer (21%) or aneuploidies (abnormal number of chromosomes) (18%). Common shortcomings among these analyses included lack of specifying the economic perspective, lack of discussion of potential bias, and lack of disclosure of funding sources.²¹⁷

As pertains to other interventions that involve the use of laboratory results to inform patient management decisions, the cost-effectiveness of PGx is subject to multiple factors or conditions. One paper suggested that a PGx strategy is likely to be cost-effective when:

- The polymorphism under consideration is prevalent in the population and has a high degree of penetrance.
- Genetic testing is highly sensitive and specific, and less costly alternative tests that could be used to individualize therapy are not readily available.
- The disease state involves outcomes with significant morbidity or mortality if left untreated.
- The treatment involves significant outcomes and/or costs that can be affected by genotype-individualized therapy.²¹⁹

As such, PGx strategies are not practical for all drug prescribing or dosing regimens, and decisions to invest in developing genomic-based therapies should be determined on a case-by-case basis.

⁸ One review, not discussed here, only addressed molecular genetic testing in familial cancers.²¹⁴ Two reviews were restricted to predictive molecular genetic tests.^{215, 216} The remaining two reviews concerned biochemical, cytogenetic, and molecular testing.^{217, 218}

CEA of Laboratory Tests: Four Examples

Compared to therapeutic interventions and other diagnostic interventions, the literature on CEA of laboratory testing is small, although a stronger literature on how to apply CEA to laboratory testing is emerging.²²⁰ The following are examples of CEAs of four types of clinical laboratory tests that have been under economic scrutiny by payers, clinicians, and other stakeholders. These examples illustrate how CEAs are conducted and reported across diverse population groups and indications, as well as the range of results of such analyses, including some suggesting that certain tests are good value for money and others that are not, at least based on incremental cost effectiveness ratio (ICER). The four examples are: screening for *Chlamydia trachomatis*, immunoassay fecal-occult blood testing for colorectal cancer, HER-2/neu testing of breast cancer, and nucleic acid testing (NAT) for safety of donated blood. The example of immunoassay fecal-occult blood testing includes discussion of how this rare request by CMS for a CEA was made and how it was used in a Medicare coverage determination.

Chlamydia Screening

The literature on economics of laboratory testing recognizes that cost-effectiveness of a given test can vary by the frequency and ordering of tests as well as characteristics of the target population. A CEA published in 2004 compared alternative strategies for screening for *Chlamydia trachomatis*, which clinical guidelines have recommended be conducted annually in women younger than 25 years of age. Using a simulation model, this analysis compared four strategies targeted to three specific age groups (15-19, 15-24, and 15-29 years) of sexually active women in the U.S.: 1) no screening, 2) annual screening for all women, 3) annual screening followed by one repeated test within 3-6 months after a positive test result, and 4) annual screening followed by selective semiannual screening for women with a history of infection.²²¹

This simulation showed that the most cost-effective strategy was annual screening in women 15-29 years of age, followed by semiannual screening for those with a history of infection. This strategy consistently had an ICER less than \$25,000 per QALY compared with the next most effective strategy. All of the strategies became more cost-effective when the indirect transmission effects of a 10-year screening program on the probability of infection in uninfected women (that is, per-susceptible rate of infection) were incorporated into the simulation. Results of the simulation were sensitive to such factors as the annual incidence of chlamydia, probability of persistent infection, screening test costs, and costs of treating long-term complications. Accounting for feasible variations in these factors in a large number of simulated scenarios, the strategy of annual screening in women 15-29 years of age followed by semiannual screening for those with a history of infection maintained an ICER less than \$50,000 per QALY in 99% of the simulations.

A systematic review published in 2006 sought to produce comparable estimates of relative health impact and cost-effectiveness for services deemed effective by the USPSTF and DHHS Advisory Committee on Immunization Practices. The review found that screening young women for chlamydia has an ICER less than \$15,000 per QALY.²²² The investigators concluded that screening young women for chlamydia was one of the most valuable clinical preventive services that can be offered in medical practice.

Immunoassay Fecal-occult Blood Testing

CEAs can be used to inform coverage decisions by public and private sector third-party payers. Although this is rarely done for the Medicare program, CMS requested that AHRQ conduct a comparative clinical and cost-effectiveness study regarding screening immunoassay fecal-occult blood testing (iFOBT) for a coverage review in 2003.²²³ Medicare was already covering colorectal cancer screening with a payment level of \$4.50 for the standard guaiac-based fecal-occult blood test (gFOBT).

AHRQ tasked this study to a team of investigators at Erasmus University, Memorial Sloan-Kettering Institute Cancer Center, and the National Cancer Institute. The investigators used a micro-simulation model to derive cost-effectiveness estimates. The analysis compared iFOBT (priced at the manufacturer-recommended amount of \$28) to two gFOBTs, Hemocult II[®] and Hemocult Sensa[®], at the Medicare reimbursement of \$4.50.^h The sensitivities and specificities of the tests were varied according to their most likely values based on an extensive literature review. The investigators found that:

- Assuming sensitivities of 40%, 70%, and 70% for Hemocult II[®], Hemocult Sensa[®], and iFOBT respectively, iFOBT would detect more cancers than Hemocult II[®] and a similar number of cancers as Hemocult Sensa[®].
- All FOBTs were cost-effective. Hemocult II[®] at \$4.50 had a cost-effectiveness ratio of \$1,071 per life-year gained and iFOBT at \$28 had a cost-effectiveness ratio of \$4,500 per life year saved, assuming 100% compliance. (Lower levels of compliance would increase the cost per life-year gained.)
- At \$28 for iFOBT and \$4.50 for Hemocult II, the ICER for iFOBT was \$11,000 per additional life-year saved, assuming 98% specificity for iFOBT, and \$21,000 per additional life-year saved, assuming 95% specificity for iFOBT.
- Compared to Hemocult II[®] gFOBT at \$4.50, iFOBT would have an equal cost-effectiveness if priced at \$13 with the more favorable assumption of 98% specificity.²²⁴

In the conclusion of its decision memorandum, CMS stated: “While the unit cost of iFOBT is generally higher than gFOBT, both are considered cost-effective compared to other cancer screening tests.” Noting that the major challenge of colorectal cancer screening was to increase compliance from current low levels, CMS added that “It is likely that simple interventions to increase compliance would be highly cost-effective as well.” The decision summary stated that “CMS concludes that there is adequate evidence to determine that the iFOBT is an appropriate and effective colorectal cancer screening fecal-occult blood test for Medicare beneficiaries aged 50 years and older.”

HER-2/neu Testing

The use of PGx to direct the use of therapies for targeted populations, especially where the therapies are expensive and where the burden of disease is great for the affected population, calls for careful weighing of health and economic tradeoffs. An instructive example of this

^h The analysis assumed that screening was confined to people aged 65 years and older, with a base case compliance level of 100%.

consideration involves testing HER-2/neu status in women with newly diagnosed breast cancer for informing the use of trastuzumab (Herceptin) for treatment of those with HER-2/neu positive breast cancer. HER-2/neu gene testing limits the risk that patients whose breast cancers do not overexpress HER-2/neu will experience potentially serious side effects of treatment with Herceptin and helps to avoid associated costs.

Two tests are used for HER-2/neu testing: immunohistochemical assays (IHC) and fluorescence in situ hybridization (FISH). These tests have different mechanisms; IHC detects protein overexpression and FISH detects gene amplification. Decisions about using these tests involve tradeoffs between the additional costs associated with using FISH and the higher rate of false-positive results associated with IHC.

A Canadian study published in 2007 compared the cost-effectiveness of various strategies of testing HER-2/neu status in women with newly diagnosed breast cancer for informing the use of trastuzumab for treatment of those with HER-2/neu positive breast cancer.²²⁵ The study involved a systematic review and meta-analysis of data comparing the agreement of IHC and FISH testing to determine HER-2/neu status. The investigators calculated the accuracy and incremental cost per accurate diagnosis for alternative testing strategies compared with the base strategy of IHC testing, followed by confirmation of 2+ scores (where the range of such scores is 0, 1+, 2+, 3+) by FISH. They observed that the median percentage of patients in each category of IHC score was: 0: 36.1%; 1+: 35.5%; 2+: 12.0%; and 3+: 16.2%. The median percentage of results of FISH that were positive in each IHC category was: 0: 1.6%; 1+: 4.9%; 2+: 29.8%; and 3+: 92.4%. The base strategy was expected to determine correctly the HER-2/neu status of 96% of patients with breast cancer. Compared to the base strategy, confirmation of HER-2/neu status by FISH in cases that received a score of 3+ reduced the percentage of false positive results to 0% and increased the percentage of accurately determined HER-2/neu results to 97.6%. This yielded a median ICER of CA\$6,175 per case of accurately determined HER-2/neu status compared to the base strategy. In comparison, the strategy of performing FISH testing in all cases of breast cancer yielded a median ICER of CA\$8,401 per case of accurately determined HER-2/neu status. The investigators concluded that the strategy with the lowest cost-effectiveness ratio involved screening all newly diagnosed cases of breast cancer with IHC and confirming scores of 2+ or 3+ with FISH.

According to a CEA published in 2004 of HER-2/neu testing and trastuzumab for metastatic breast cancer, IHC with confirmatory FISH testing resulted in an ICER of \$125,000 per QALY and initial FISH testing (without IHC) resulted in an ICER of \$145,000 per QALY.²²⁶ These ratios are higher than the \$100,000 per QALY level cited as an informal acceptable threshold in the U.S. by some health economists²²⁷ and thresholds cited in western Europe and certain other industrialized countries. Even so, these ICERs for HER-2/neu testing are of similar or lesser magnitude than those for various other cancer therapies and many other widely used health care interventions. Continued improvements in testing, targeted treatments and lower costs that may arise with competing interventions should improve the cost-effectiveness of HER-2/neu testing and related tests for breast cancer.¹⁵⁴

A study published in 2007 modeled the incremental cost-effectiveness of adding trastuzumab to chemotherapy regimens in patients with HER-2/neu-positive breast cancer. The model assumed that both IHC and FISH were used to determine HER-2 status. The study assumed that, on average, five tests were performed for every patient identified for trastuzumab treatment; 30% of

tests were assumed to be FISH in the base case. While this study did not analyze the cost-effectiveness of the testing in particular, it projected that the incremental cost per QALY gained of adding trastuzumab to chemotherapy, including the cost of testing to inform the therapeutic decision, was \$26,417. The cost-effectiveness of treatment with trastuzumab over a 20-year horizon was projected to be \$34,201 per QALY gained.²²⁸

Nucleic Acid Testing for Blood Safety

As described above, the accessibility of safe blood is vital for millions of people in the U.S. The blood supply is rigorously screened and tested throughout the collection and transfusion process. Scientific and technological advances have led to continued improvements in the safety of the blood supply, so that transmission of infectious agents of greatest concern to health – HIV and hepatitis B and C viruses – is rare. Recent advances have focused on decreasing the “window period” of detecting viral antibodies and antigens, so as to diminish the chances of failing to detect infected blood donations shortly after donors have contracted the pathogen. To the extent that newer, more sensitive tests become available, any additional cost of detecting incrementally more cases raises questions about the cost-effectiveness of these tests.^{i,206}

NAT, which relies on polymerase chain reaction techniques, can detect the presence of viral genes in blood. NAT can be conducted on “minipools” of 16-24 samples (minipool NAT) or on individual donations of blood (individual donation NAT). Alternative testing strategies can yield significantly different cost-effectiveness ratios. NAT has been the topic of several CEAs.

Based on detailed CEAs, researchers have concluded that use of NAT to screen all donated blood for HIV and hepatitis C virus results in ICERs of more than \$5 million per QALY saved. In addition to the cost of testing many units of donated blood for the rare ones that cannot be detected by other means, the short life expectancy of many people who receive donated blood products constrains the health impact, and therefore the cost-effectiveness, of successful testing.²⁰³ A CEA published in 2003 examined the marginal cost-effectiveness of using NAT for HIV and hepatitis B and C viruses in whole-blood donations using 2001 disease incidence data from the American Red Cross.²³¹ This study estimated that the addition of minipool NAT to HIV antigen testing would add a total of 62 QALYs per year in the U.S., while the addition of individual donation NAT would add a total of 90 QALYs per year. The cost per QALY gained for adding individual donation NAT in addition to HIV antigen testing ranged from \$8.4 million to \$9.1 million, depending on whether hepatitis B virus testing was included.^j Eliminating HIV antigen testing and using only NAT would reduce costs, but cost per QALY gained would remain above \$4 million. The investigators concluded that the cost-effectiveness of adding NAT to serologic testing is poor.

An analysis published in 2004 examined the cost-effectiveness of adding either individual donation NAT or minipool NAT to pre-existing serologic testing protocols for HIV and hepatitis B and C viruses with scenarios that included and excluded HIV antigen testing for blood donated in

ⁱ As is so for many other avenues of health care, the increases in the safety of the blood supply achieved with additional testing have represented diminishing returns over time.²⁰³ Whereas the ICER of HIV antibody testing, implemented in 1985, was less than \$5,000 per QALY saved,^{229, 230} the ICER for HIV p24 antigen testing, introduced in 1996, was estimated to exceed \$2 million per additional QALY saved.

^j Adding minipool NAT to HIV antigen testing would result in a cost per QALY gained ranging from \$5.8 million to \$7.6 million, depending on whether or not a test for hepatitis B virus was included.

the U.S. Compared with serologic testing alone, minipool NAT was found to save a total of 102 additional QALYs and individual donation NAT was found to save an additional 115 QALYs. Serologic testing (excluding HIV antigen testing) coupled with minipool NAT resulted in an ICER of \$1.5 million per QALY gained. Serologic testing (excluding HIV antigen testing) in conjunction with individual donation NAT was found to be associated with an ICER of \$7.3 million per QALY gained. This study confirmed that the cost-effectiveness of adding NAT to current serological testing far exceeds the traditionally recognized, though informal in the U.S., threshold of \$50,000 to \$100,000 per QALY gained. The authors concluded that the cost per QALY of adding NAT screening is beyond the typical range for most health care interventions, but not for established blood safety measures.²³²

Notwithstanding its unfavorable cost-effectiveness, NAT screening has been widely adopted. The American Red Cross uses minipool NAT to test for HIV in all donated blood. The main justification for implementing NAT screening was the concern of the public and policy makers arising from the potential, however rare, for patients to contract a catastrophic illness from the blood supply.^{231, 232}

CONCLUSIONS

Laboratory testing is integral to many clinical decisions, providing physicians, nurses, and other health care providers with often pivotal information that aids in prevention, diagnosis, treatment, and management of disease. Despite their impact, spending on laboratory services accounts for only 2.3% of health care expenditures and 2% of Medicare expenditures.

- Laboratory medicine supports the practice of evidence-based medicine and development of clinical practice guidelines, which assist practitioners and patients in making decisions about health care in specific circumstances.
- Laboratory tests provide objective data about patient health that enable screening for risk factors, accurate and early diagnosis, determination of disease severity and likelihood of recovery, selection and monitoring of treatment, and evaluation of potential adverse outcomes. Laboratory tests also are vital to patient self management of chronic conditions, supporting their ability to monitor their health status daily, adjust therapies, and evaluate progress with healthy lifestyle choices.
- Information provided by laboratory testing is a critical component of quality and safety, including the prevention of adverse reactions. Laboratories protect the blood supply from pathogens and accurately match patients and blood products. For managing medication, testing provides information for maintaining optimum drug levels, helps to detect and recover from medication errors, and enables use of genetic information to guide personalized health care.
- Laboratory testing is incorporated into indicators used to assess quality of care, particularly for diseases of high health and economic burden such as diabetes, heart failure, and colon cancer. Laboratory data also can be used in new and emerging approaches to value-based purchasing of health care.
- The evidence base for the cost-effectiveness of laboratory tests, and the broader therapeutic regimens and other interventions of which they are a part, is growing, though still limited. This evidence is helping to inform test selection and sequencing, technology acquisition

decisions, formulary design (including for PGx-mediated therapies), and screening and other population-based interventions. Though used less in the U.S. than in other developed nations, it is being considered in selected coverage and payment policies of some health plans and other third-party payers.

- Services provided by clinical laboratories also are critical to public health at the individual and population levels by identifying nosocomial infections, antimicrobial resistance, infectious disease outbreaks, exposure to toxic substances, and chemical and biological threats. Laboratories also help to mitigate the effects of natural disasters by enabling rapid turnaround of tests used during triage and emergency care of individual patients as well as tests to confirm the presence of communicable diseases that threaten the population.
- Consistent with other sectors of health care, laboratory medicine is under greater scrutiny for demonstrating its value for patients, providers, payers, and other stakeholders. Value must be documented based on rigorous clinical, public health, and economic evidence. Whether in the form of quality indicators, practice guidelines, coverage policies, value-based purchasing or related payment policies, or simply market share for laboratory services, the value of laboratory medicine is being explicitly incorporated into health care decisions.

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CHAPTER II

MARKET PROFILE OF THE LABORATORY MEDICINE SECTOR

This chapter provides an overview of the size and structure of the U.S. laboratory sector, including revenue, spending, test volume, and other key elements. Market information is delineated by laboratory setting and test type. Settings include hospitals, physicians' offices, other clinical settings (e.g., skilled nursing facilities), and independently operated sites in the community. Examining market by test type highlights trends in the traditional broad disciplines of clinical pathology and anatomic pathology as well as the emerging interdisciplinary areas associated with molecular pathology. Depending on the type of test and the state of origin, consumers may perform self testing at home, work, or another site, or order tests directly through a clinical laboratory or the Internet.

Publicly available information about the economic status and quality of the laboratory medicine sector is limited. For purposes of this chapter, data were compiled from multiple public and private sector sources. Among these sources were market research reports, such as *Lab Industry Strategic Outlook: Market Trends and Analysis 2007*^a, the CMS OSCAR database, which contains information about laboratory certification, accreditation, and proficiency testing; other government reports; published literature; and personal communications with industry experts and government officials.

U.S. MARKET SIZE

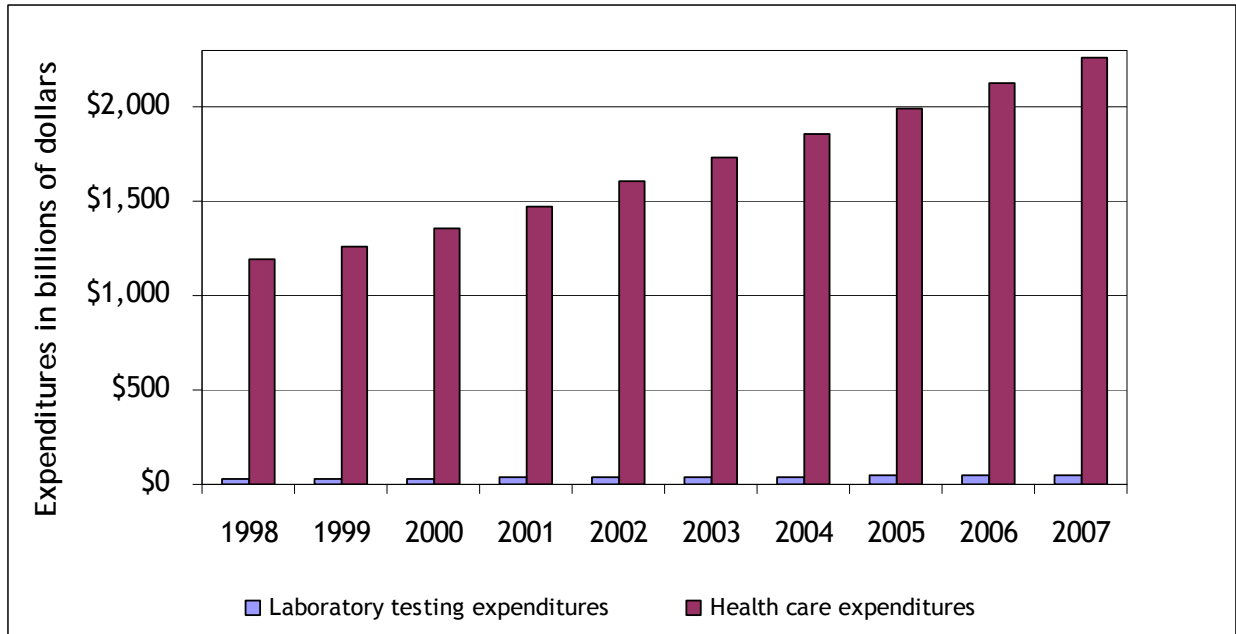
The revenue, spending, and test volume of the U.S. clinical laboratory testing market has grown steadily over the past decade. Market data indicate that:

- Revenues have increased by more than 40% since 1998 (not adjusted for inflation). In 2006, laboratory industry revenues (i.e., gross earnings) were valued at approximately \$48.5 billion, with predicted growth of 6.5% to \$51.7 billion in 2007.¹
- Spending growth on clinical laboratory services averaged 7% annually over the 2003 to 2006 period, just slightly less than the growth rate in total national health care spending at 8%.¹ However, laboratory expenditures as a percentage of total health care spending have remained relatively stable at 2 to 3% from 1998 to 2007 (see Figure 2.1).

^a *The Lab Industry Strategic Outlook: Market Trends and Analysis*, published by Washington G-2 Reports, compiled data from its own surveys; proprietary surveys of hospitals and independent laboratories; data from CMS; financial reports filed with the Securities and Exchange Commission; population and business data from the U.S. Census Bureau; and interviews with laboratory industry executives, hospital laboratory managers, consultants, and government executives. One of the surveys conducted for the 2007 report was sent to 12,000 laboratories in their database, of which 141 responded. Approximately 55% of respondents were hospital/health system laboratories, 17% were independent or commercial laboratories, 2% were pathology groups, 7% were POLs, and 19% were categorized as "other" (i.e., a combination of one or more type of laboratory). However, because of the very low response rate, the results of this survey may be limited in terms of generalizability to the larger laboratory sector.

- *Total volume* of laboratory testing was projected to be approximately 6.8 billion tests in February 2008, according to data self reported by laboratories and compiled in the CMS OSCAR database.² However, higher figures have been reported by another organization.^b

Figure 2.1: Total Health Care and Laboratory Expenditures, United States
1998 - 2007



Sources: Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

National health expenditures by type of service and source of funds: CY 1960-2005. Baltimore, MD: Centers for Medicare and Medicaid Services, 2007. (Accessed July 23, 2007, at http://www.cms.hhs.gov/NationalHealthExpendData/02_NationalHealthAccountsHistorical.asp#TopOfPage.)

National health expenditures projections 2006-2016, forecast summary and selected tables. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006. (Accessed July 23, 2007, at http://www.cms.hhs.gov/NationalHealthExpendData/03_NationalHealthAccountsProjected.asp#TopOfPage.)

Many factors contribute to market growth in the laboratory sector, including:

- *Aging of the population* and corresponding increase in the prevalence of chronic diseases, which are highly dependent on use of laboratory testing and services for diagnosis, treatment, and ongoing management. More than 90 million Americans live with chronic illnesses, and about half of adults aged 65 and older live with at least two chronic medical conditions.^{3,4}
- *Growth of the U.S. population* from 266 million in 1997 to 301 million in 2007, a 13% increase that has contributed to higher rates of spending on laboratory tests.^{1,5,6}

^b The true number of laboratory tests conducted annually in the U.S. is not known. A 1996 report published by the National Inventory of Clinical Laboratory Testing Services estimated the annual number of tests to be 7.25 billion. Using the OSCAR database, CDC estimated annual volume at 6.8 billion tests in February 2008 (as cited above).² Yet, there are some limitations to the data. First, laboratories with a certificate of waiver usually do not provide updates of test volume after the initial application. Second, OSCAR data is self-reported by laboratories and is not confirmed by CMS or any other organization. Lastly, CLIA may count tests differently than other laboratories or other organizations (e.g., for chemistry profiles, CLIA counts each individual analyte separately).

Approximately 60% of this population growth is attributed to the net difference between birth and death rates; 40% is attributed to immigration.⁷

- *Research in molecular diagnostics* and development of new tests in the areas of genomics and proteomics to support more targeted clinical care.^{8,9} The U.S. government continues to devote great resources to expand research beyond the Human Genome Project. Such efforts are complemented by a vibrant, innovative private sector.
- *Continued miniaturization* of testing equipment, increasing use of point-of-care devices, and development of high-throughput automated systems. Great advances in miniaturization of assay technologies enable more efficient, high-volume testing.^{10,11}
- *Increased incorporation of laboratory testing as an indicator* of quality of care and provider performance. Evidence continues to accumulate on the association of biomarkers with health care outcomes of interest to consumers, purchasers, and payers.^{12,13}
- *Increased media attention* to health-related issues has increased consumer awareness of and requests for certain laboratory tests.^{1,14} For example, a 2003 report by CDC found that providers in metropolitan areas where a genetic test for breast and ovarian cancer susceptibility was marketed directly to consumers ordered more tests.¹⁵

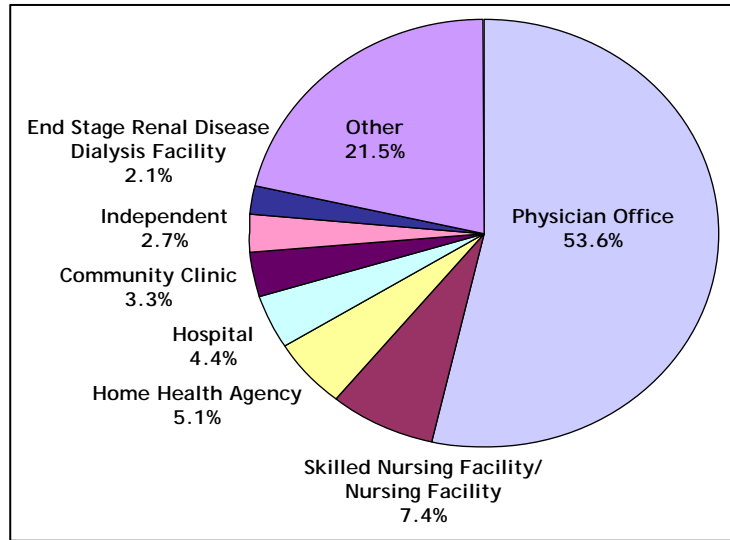
MARKET BY LABORATORY TYPE AND SETTING

Laboratory types vary according to their settings, including hospitals, POLs, independent laboratories, and public health laboratories, among others. Laboratories must register with CMS, obtain the appropriate certificate, and comply with CLIA requirements. Under CLIA, laboratory tests are categorized as either waived or non-waived. Laboratories performing waived^c testing must obtain a certificate of waiver (CW), while those conducting non-waived PPM must obtain a certificate for PPM procedures. Laboratories conducting other non-waived testing must obtain a certificate of compliance (COC) following inspection or a certificate of accreditation (COA) from a CMS-approved private sector accreditation organization.

The number of CLIA-certified laboratories in the U.S. has increased steadily since implementation of the regulations. The number of laboratories grew 28% from 154,740 in 1993 to 198,232 in 2006.¹⁶ According to CMS, there were 203,939 CLIA-certified laboratories providing testing services in the U.S. as of December 2007.¹⁷ Figure 2.2 depicts the breakdown of the most common laboratories by type.

^c Waived tests are those whose methods are judged to be sufficiently simple and accurate that the likelihood of erroneous results is negligible, that they pose no reasonable risk of harm to the patient if performed incorrectly, and that have been cleared by FDA for home use.

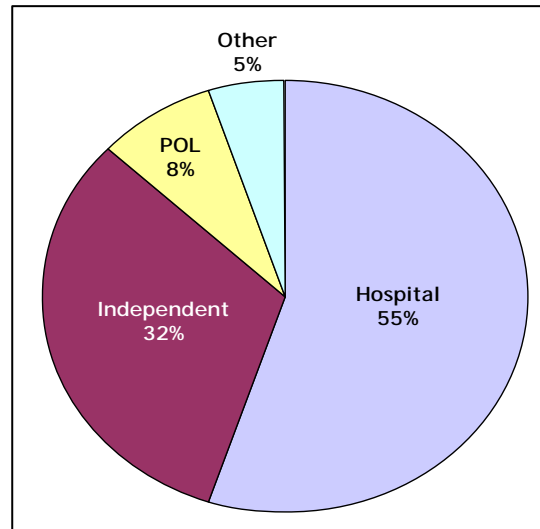
Figure 2.2: Most Common Types of Laboratories, 2006



Source: CLIA update—December 2006, laboratories by type of facility. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006.

Although the raw number of hospital laboratories displayed in Figure 2.2 is relatively small, they held the largest market share by both test volume and revenue in 2006, as presented in Figure 2.3.¹ Independent laboratories had the second-highest market share, followed by POLs.

Figure 2.3: U.S. Laboratory Industry Market Share by Test Volume, 2006



Source: CMS-CLIA laboratory application forms. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Hospital-based Laboratories

Hospital laboratories are the chief provider of laboratory services for their inpatient population as well as outpatient population receiving care from physicians who are affiliated with the hospital.¹⁸ Outpatient laboratory testing is conducted on patients who are receiving care from providers affiliated with the hospital but who have not been admitted to the hospital. Also, hospital laboratories often conduct outreach testing, serving as the reference laboratory for others in the community with limited testing capabilities.¹

In 2006, there were 8,680 hospital-based clinical laboratories in the U.S., which together conducted about 3.3 billion laboratory tests.^{16,19} The number of hospital laboratories increased by 6% between 2000 and 2004, but decreased by 0.8% between 2004 and 2006 due to competition from independent laboratories and consolidation through mergers and acquisitions.¹ Generally, the number of hospital-based laboratories exceeds the number of hospitals (5,756 hospitals in 2006).^{20,21} In addition to a main laboratory, hospitals may operate laboratories in their emergency department, intensive care unit, pulmonary service, surgical service, and satellite sites.²²⁻²⁴

Revenue. In 2007, revenues for hospital laboratories are projected to reach \$28.4 billion, an increase of more than 6% over 2006.¹

Volume. In 2005, hospital test volume grew by a median of 5% and an average of 6% over 2004, including inpatient and outpatient testing.¹ Hospital laboratories with the lowest test volumes (fewer than 250,000 tests per year) had the highest growth rates (see Table 2.1).

Table 2.1: Hospital Laboratory Median and Average Test Volume Growth, 2005

Annual Volume	Median Growth	Average Growth
<250,000	6.4%	7.5%
250,000 - 499,999	4.3%	5.6%
500,000 - 999,999	5.0%	5.9%
≥1 million	5.0%	6.7%
Overall	5.0%	6.4%

Source: Reprinted with permission from Washington G-2 reports. *Third annual outreach survey*. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Budget. A 2005 survey of laboratories found that about 36% of hospital laboratories operated with a budget of less than \$5 million per year, while the budget of another 37% was between \$5 million and \$20 million.¹ Over one-third of these budgets is spent on staff salaries, more than 20% on supplies, nearly 9% on employee benefits, and approximately 7% on blood-related expenses. The remaining 30% is devoted to rent, repairs, internal test transfers, and other expenses. About half of the laboratories responding to the survey cited staff salaries as the fastest-growing component of their budgets.¹

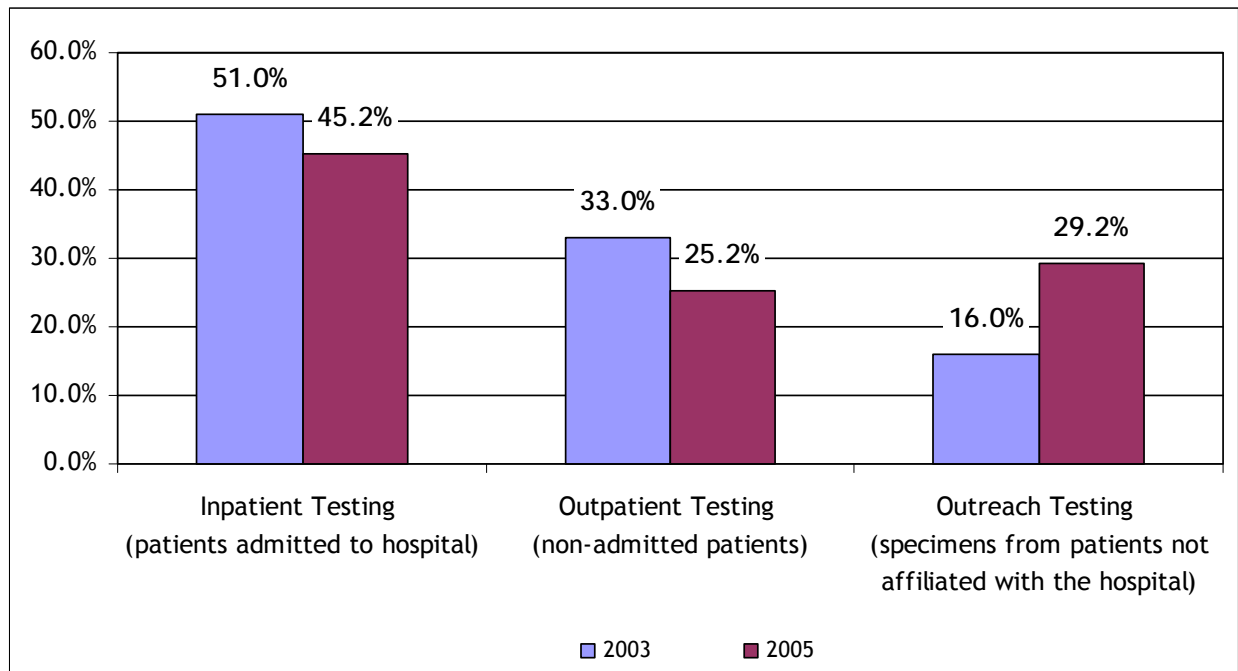
Staff. Approximately 60% of laboratory technologists/scientists^d and 43% of technicians worked in laboratories based in general medical and surgical hospitals in 2006.^{25, 26} The percentages of these professionals employed in general medical and surgical hospitals has remained steady since 2002.

Hospital Outreach Testing

Hospital laboratories that perform outreach testing function as reference laboratories for other hospitals, community clinics, POs, and other facilities.²⁷ Specimens tested through outreach services are rarely collected by the outreach laboratory itself.²⁸

Hospitals have marketed outreach testing services to generate additional revenue and compete with independent laboratories. While 74% of hospital laboratories actively marketed their outreach services in 2003, 91% marketed these services in 2005.¹ Outreach testing volumes increased from 16% of hospital laboratory testing volume (2003) to 29% (2005) as a result of these marketing activities. Profitability has risen as well – nearly 85% of hospital laboratory outreach programs surveyed in 2005 reported a profit. Figure 2.4 provides a comparison of hospital inpatient, outpatient, and outreach testing.

Figure 2.4: Components of Hospital Laboratory Testing, 2003 and 2005

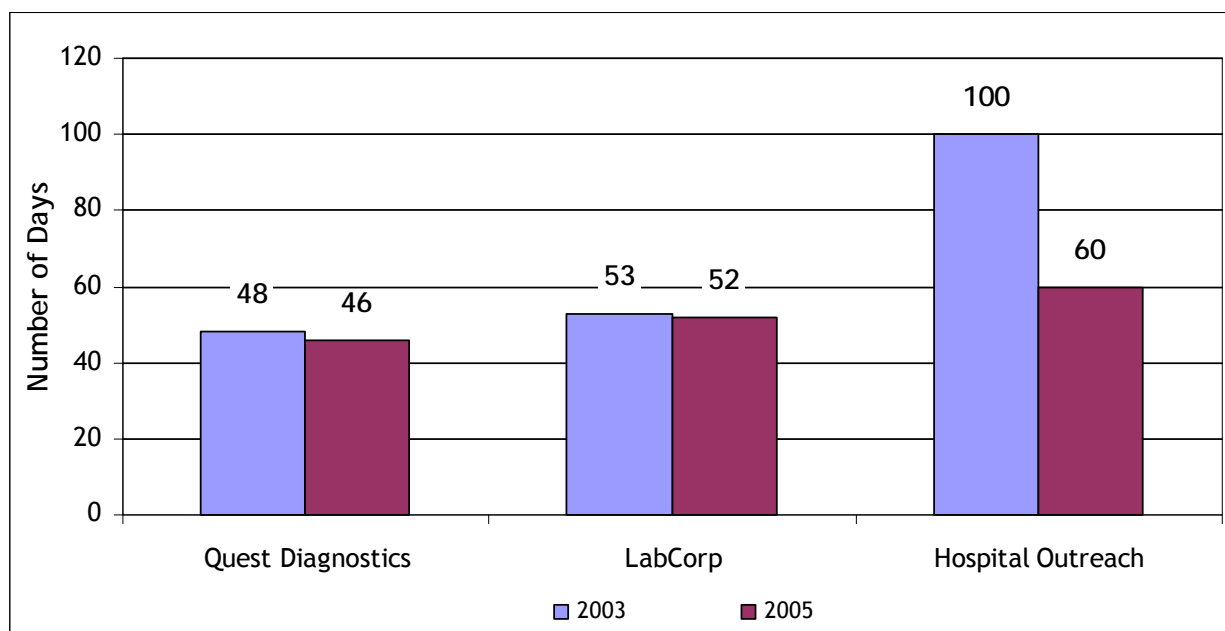


Source: Reprinted with permission from Washington G-2 reports. *First national hospital laboratory survey and third annual outreach survey*. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

^d Clinical laboratory technologists/scientists conduct laboratory tests on tissues, blood, and other bodily fluids and perform a full range of complex chemical, biological, hematological, and immunologic tests. Laboratory technicians work under the supervision of a technologist/scientist and conduct less complex tests in all areas of the laboratory.

To further increase competitiveness, many outreach laboratories have invested in Internet connectivity, improved billing and pricing of tests, and focused on faster test TATs. The efficiency of their billing systems is close to that of their competitors.¹ Efficiency gains, as determined by the number of days in accounts receivable,^e are depicted in Figure 2.5. In 2006, more than 45% of hospital outreach laboratories reported that they were holding their market share and 38% reported that they were gaining market share.

Figure 2.5: Median Days in Accounts Receivable, 2003 versus 2005



Source: Park City Solutions (now Chi Solutions, Inc.). *Fourth comprehensive national laboratory outreach survey 2005*. Ann Arbor, MI: Chi Solutions, Inc., 2005.

Reprinted with permission from Washington G-2 reports. *First national hospital laboratory survey and third annual outreach survey*. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Physician Office Laboratories

POLs comprise the largest portion of clinical laboratories in the sector. As of December 2006, there were 106,190 POLs, about 54% of the total number of CLIA-certified laboratories in the U.S.¹⁶ From 2000 to 2006, the number of POLs increased 12% and the total number of all laboratories increased by approximately 17%.^{16,30}

Testing in POLs tends to be limited to a small number of specimens and is often conducted by medical assistants.³¹ On-site testing in POLs allows for immediate availability of results to clinicians.^{21,32} More than 80% of POLs are certified to perform only waived and/or PPM tests.¹ However, some POLs that serve large group medical practices are certified to perform certain

^e Days in accounts receivable can be calculated by determining the number of days between date of service to date of payment and averaging across all claims or by calculating the ratio of accounts receivable to average daily charges and multiplying by 365 days.²⁹ Days in accounts receivable measures a company's billing efficiency; a higher figure is inversely related to lower billing efficiency.¹

moderate and high complexity tests that are typically provided by hospital and independent laboratories.

Data provided by the American Academy of Family Physicians estimate that nearly 50% of testing conducted in family physician POLs is waived, 13% of testing is PPM, 22% is moderate complexity (e.g., tests to measure theophylline levels), and 4% is high complexity (e.g., tests to measure antibiotic susceptibility).³³ Tests commonly performed in family physician POLs are highlighted in Table 2.2.^f

Table 2.2: Ten Most Commonly Offered Laboratory Tests at Family Physician's Offices and Percent of Offices Performing Test On-Site, 2005

Name of Laboratory Test	Percent of Physician's Offices Performing Test On-Site
Dipstick/tablet urinalysis	97.5%
Fecal occult blood	92.2%
Urine pregnancy test	87.2%
Rapid strep (direct antigen)	86.5%
Vaginal smear/wet mount	76.6%
Glucose, using a waived instrument	68.3%
Urine microscopic exam	61.1%
Infectious mononucleosis screen	39.2%
Prothrombin time	39.0%
Glucose, visual whole blood glucose dipstick (performed via fingerprick)	35.3%

Sources: American Academy of Family Physicians. Performance of laboratory services in family physician practice settings. Practice Profile II Survey, October 2006. Leawood, KS: American Academy of Family Physicians, 2006.

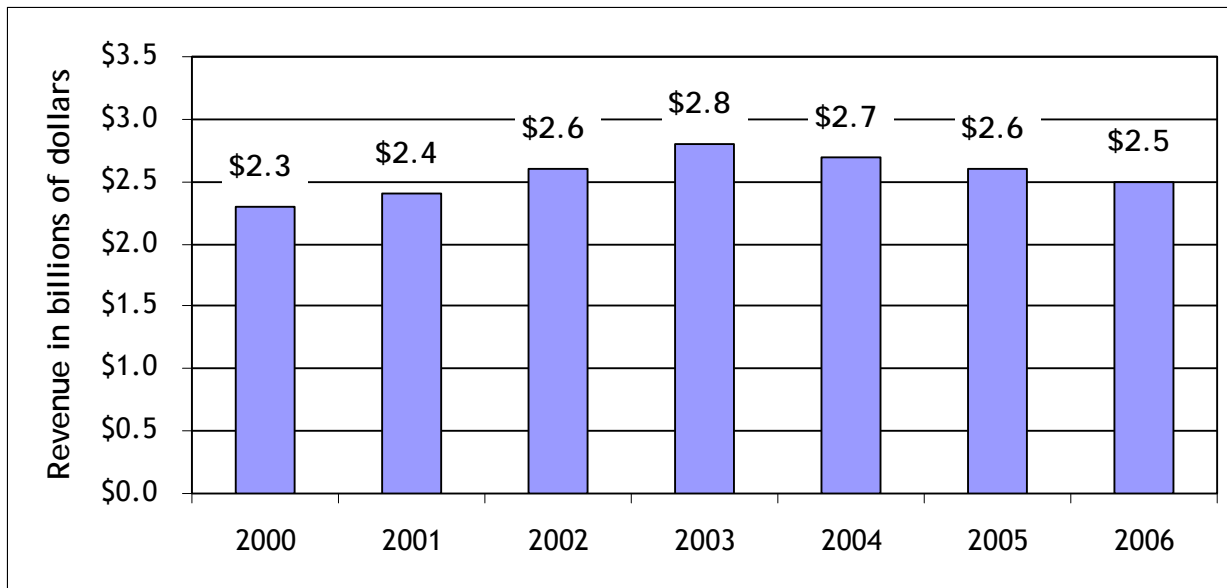
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Revenue. In 2006, POLs generated \$2.5 billion in revenues, comprising 5% of total revenues for the industry. Revenues from POLs increased between 2000 and 2003 by approximately 22%; however, slowed growth in the number of POLs is reflected in the small but consistent revenue declines since 2003 (see Figure 2.6). Decreasing revenue also is attributed to shifts in the types of, and payments for, tests provided by POLs. Manufacturers have significantly increased the availability and marketing of waived tests to POLs, promoting ease of use, point-of-care access to test results, and convenience for the patient. The shift toward less expensive testing also has been fueled by declining reimbursement rates. Medicare reimbursement for the top 20 tests provided by POLs in 2006 averaged almost \$1.00 *less* than that for the top 20 POL tests in 2002.^{g1}

^f Dipstick urinalysis, fecal occult blood, and streptococcal antigen detection also were among the top five most commonly offered tests according to two surveys, one conducted in 2003 by CMS of CW sites and one conducted of pediatric-based POLs in 1996 by the Illinois chapter of the American Academy of Family Physicians.^{34, 35}

^g This comparison was based on the difference between the average reimbursement for the top 20 tests in 2002 and 2006; the sets of top 20 tests differed in the two years.

Figure 2.6: Physician Office Laboratory Revenue, 2000 - 2006



Source: Reprinted with permission from Washington G-2 Reports. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Volume. POLs conduct an estimated 525 million laboratory tests annually; approximately 29.5% of these tests are waived.¹⁹ POLs accounted for approximately 8% of the total number of laboratory tests performed in the U.S. in 2005, a decrease of 3% from 2003.¹

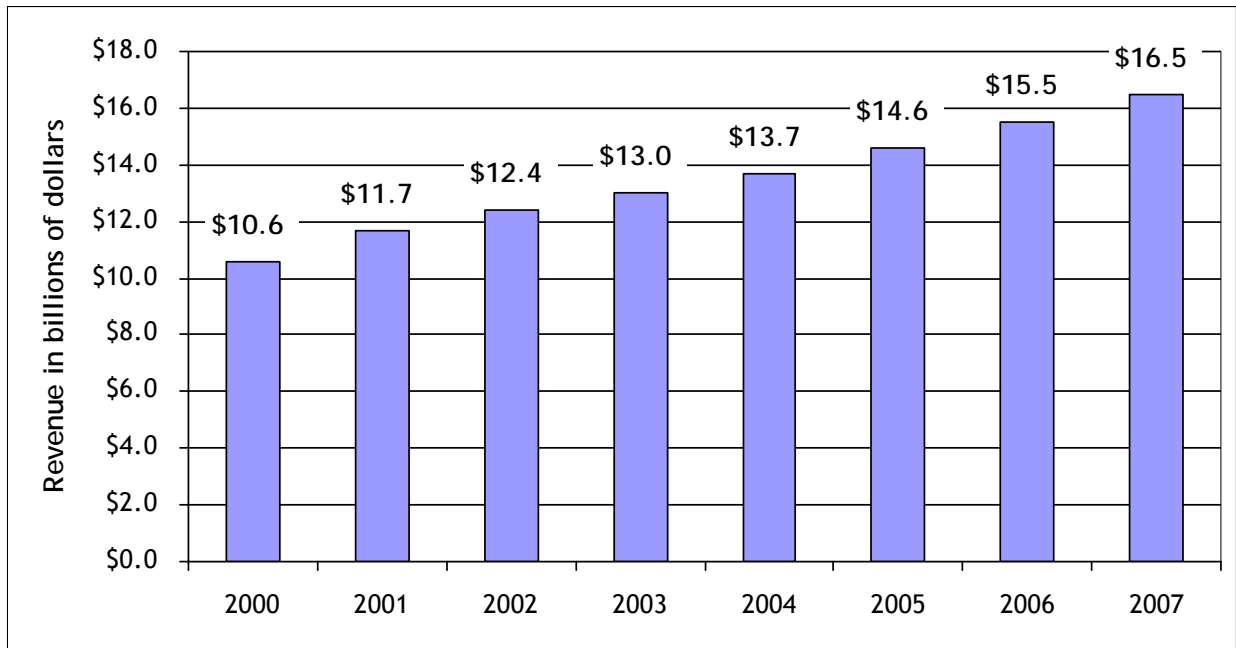
Staff. From 2002 to 2005, the proportion of the clinical laboratory workforce employed in POLs declined, including a drop from 10% to 8% for technologists/scientists and 18% to 17% for technicians (i.e., as a percentage of all technologists/scientists and technicians in the U.S.).^{25, 26, 36, 37} This decrease may be due to slower revenue growth among POLs (and subsequently, fewer funds available for salaries) between 2003 and 2006. The decrease in the number of skilled laboratory personnel is linked to the increase in waived testing during this time.³⁵ The decline in the number of technologists/scientists and technicians employed in POLs accompanies the increasing number of POLs holding only a CW, under which there are no personnel requirements.

Independent Laboratories

In 2006, there were 5,414 CLIA-certified, privately-owned independent laboratories in the U.S. operated by non-profit and for-profit corporations.¹⁶ Privately-owned independent laboratories conduct approximately 1.5 billion tests annually. Approximately 74% of these laboratories are certified to perform non-waived testing.¹⁹

The independent laboratory sector accounts for 32% of clinical laboratory testing and 35% of the revenue produced by the industry.¹ From 2000 to 2006, revenue produced by independent laboratories grew from \$10.6 billion to \$15.5 billion, an increase of approximately 46% (see Figure 2.7). Growth in independent laboratory revenue is expected to continue at a rate of nearly 6% to \$16.5 billion in 2007. Table 2.3 provides market data of the seven publicly traded companies with the highest revenue in the first half of 2005.

Figure 2.7: Independent Laboratory Revenue, 2000 - 2007



Source: Reprinted with permission from Washington G-2 Reports. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Table 2.3: Publicly Traded Laboratory Companies with Highest Revenue First Half of 2005

Company	Revenue First Half 2005
Quest Diagnostics	\$2.70 billion
LabCorp	\$1.65 billion
AmeriPath	\$278 million
LabOne	\$252 million
Genzyme Genetics	\$107 million
Bio-Reference*	\$76.9 million
Specialty Laboratory	\$75.7 million

*Bio-Reference's revenue is for six months ended April 30

Source: Reprinted with permission from Washington G-2 Reports. *Laboratory Industry Report* from company reports. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Market Competition. Small- and mid-sized independent laboratories, as well as hospital outreach laboratories, face significant competition from the large laboratory corporations, which have sizable financial resources and economies of scale. Eleven mid-sized independent laboratories with annual revenues between \$10 and \$500 million had combined total revenues of \$1.04 billion in 2005, a 19% increase from 2004. According to survey data, three small, independent laboratories with annual revenue of less than \$10 million estimated an increase in revenue of 15% between 2006 and 2007.¹

Several factors have contributed to the competitive advantages of the large corporations: national managed care contracts; efficient, centralized billing management; lower supply costs; extensive high complexity testing capabilities; and the ability to invest in Web-based systems. The two largest laboratories have contracts with the three largest managed care organizations (i.e., UnitedHealthcare, Cigna, and Aetna).¹ These contracts generated 42 to 50% of their total revenues in 2006.

Given their test volume, large laboratories are able to negotiate more favorable contracts with reagent and supply vendors, sometimes at costs 30 to 50% less than those paid by hospitals and smaller independent laboratories. Financial resources have allowed large laboratories to build capacity for high complexity testing, upgrade billing management systems, and invest in Web-based systems to improve efficiency in ordering, billing, and result reporting. However, the sheer size of their operations can result in disadvantages in physician communication, specimen pickup scheduling, and test TATs, areas in which smaller laboratories can excel. Smaller laboratories are often located closer to their clients, facilitating greater laboratory-client interaction. They also may offer more flexibility in scheduling specimen pickup times than large laboratories that are tied to specific times for daily specimen pick ups.¹

Public Health Laboratories

Public health laboratories are government laboratories dedicated to safeguarding the public's health.³⁸ While their responsibilities and roles intersect at many points, public health laboratories generally do not compete with private clinical laboratories because their focus is on population health and security rather than individual patient testing. Responsibilities of public health laboratories include:

- Specialized disease testing to detect and monitor newly emerging infectious diseases, such as West Nile virus, severe acute respiratory syndrome, and new influenza strains
- Newborn screening to detect potentially life-threatening metabolic and genetic disorders, such as phenylketonuria, sickle cell disease, and cystic fibrosis
- Molecular analyses to differentiate one strain of a disease organism from another (e.g., *E. coli* O157:H7, which causes foodborne illness)
- Confirmatory testing to verify the identity of microbes and other suspect agents
- Testing to detect the presence of sexually-transmitted diseases
- Testing to detect the presence of bacteria, parasites, pesticides, and other potentially harmful agents in the environment, especially drinking water
- Routine surveillance of public health threats and emergencies by analyzing samples, providing information to support effective response, and working with other health authorities to protect citizens³⁸⁻⁴⁰

State Laboratories. Public health laboratories include state and local facilities. There are a total of 56 state public health laboratories in the U.S., including one in every state and U.S. territory.^{h,41} State public health laboratories, usually part of the state health agency, are responsible for

^h U.S. territories include American Samoa, Guam, the Marshall Islands, Puerto Rico, the Mariana Islands, and the U.S. Virgin Islands.

participating in national public health surveillance activities and monitoring disease trends.³⁸ Often, state public health laboratories provide training to workers in private sector and local public health laboratories, and in some states provide regulatory oversight of clinical and/or local public health laboratories.

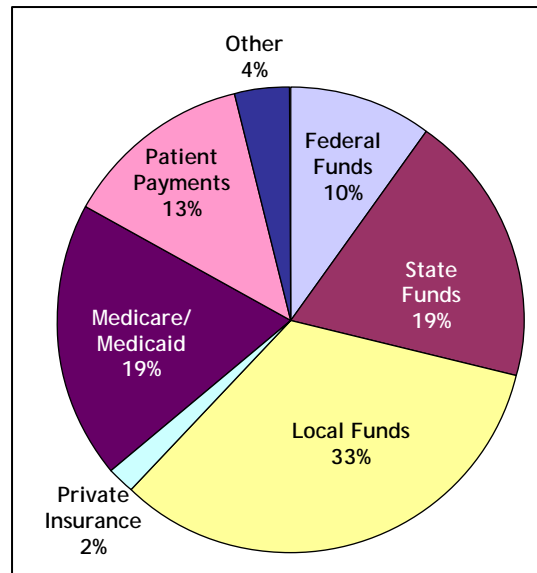
Local Laboratories. Local public health laboratories function at the city or county level. The Association of Public Health Laboratories estimates that there are between 600 and 800 local public health laboratories in the U.S. (The precise number and capabilities of these laboratories varies according to how the laboratory is defined.)⁴¹ Most states have several local public health laboratories that range from large urban laboratories employing hundreds of scientists to small rural laboratories staffed by one or two scientists.³⁹

In general, local public health laboratories have greater familiarity with local health problems and stronger ties to their communities than state-level laboratories.⁴² A 2003 survey of local public health agencies found that more than two-thirds rely on in-house public health laboratories for at least some of their testing needs. Agencies located in larger counties or cities were more likely to use their own laboratory than those located in smaller or rural locations. When testing is required beyond the local agency, the specimen is usually sent to the state public health laboratory. Other referral sites include independent laboratories, hospital laboratories, other state public health laboratories, and university laboratories.

A 2003 survey indicated that 39% of local public health laboratories were certified to perform waived testing. Of the 61% that were certified to perform non-waived testing, 39% were certified to perform moderate complexity tests and 22% were certified to perform high complexity tests, e.g., tests for the fungal disease candidiasis and the enteric pathogen shigella.⁴² Nearly 70% of testing fell into the waived category, compared to 20% for moderate complexity, and 11% for high complexity. Public health laboratories serving larger populations tended to offer higher-complexity testing.

Local public health laboratories derive revenue from a variety of sources, as shown in Figure 2.8, about half of which is provided by local and/or state governments.

State and local public health laboratories are likely to face significant challenges over the next several years. Emphasis on public health preparedness and its ability to respond quickly and effectively to biological or chemical terrorist threats has led to increased scrutiny of public health laboratory infrastructure.⁴³ Public health laboratories are being called upon to foster and lead preparedness and response planning efforts for emerging infectious diseases, such as pandemic influenza.⁴⁴ Biomonitoring, or the measurement of chemical levels in the human body (e.g., in blood, urine, or saliva) to assess human exposure to pollution is an area where state public health laboratories are continuously called upon to play a large and leading role.⁴⁵ Collaboration between public and private laboratories and continued funding of current and future initiatives will remain vital components critical to the success of public health laboratories.

Figure 2.8: Sources of Revenue for Local Public Health Laboratories, 2003

Source: Assessing America's local public health laboratory capacity. Silver Spring, MD: Association of Public Health Laboratories, 2004.

Skilled Nursing/Nursing Facility Laboratories

Skilled nursing is health or rehabilitation care that can only be provided safely and correctly by a registered nurse or licensed practical nurse.⁴⁶ According to CMS, there were 14,838 skilled nursing facilities in the U.S. in December 2003.⁴⁷ As of December 2006, a total of 14,760 skilled nursing or nursing facilities had their own clinical laboratories, comprising 7.36% of all laboratories.¹⁹ Skilled nursing or nursing facility laboratories conduct approximately 60.4 million tests annually. More than 99% of skilled nursing or nursing facility laboratories are certified to perform waived or PPM testing.

Home Health Agency Laboratories

Home health care usually refers to medical care that is provided to elderly and other patients with the goal of enabling them to regain their independence and retain the highest degree of self-sufficiency without being confined in a hospital.⁴⁸ Home health care can include skilled nursing care, physical and occupational therapy, speech-language therapy, mental health services, palliative care, and medical social services.⁴⁹ Organizations whose main function is to provide home health care services and supplies must meet federal and state requirements for licensure and certification.⁵⁰ As of March 2007, there were approximately 11,130 Medicare-certified home health agencies in the U.S.⁵¹

Many home health agencies operate their own clinical laboratories to serve the needs of their clients. In 2006, there were 10,134 home health agency-based laboratories, accounting for more than 5% of all laboratories in the U.S.¹⁹ The annual volume of testing conducted by home health laboratories is approximately 18.4 million. About 98% of testing conducted in home health agencies is waived and more than 99% of home health agency laboratories are certified to conduct waived or PPM testing only.

Other Types and Settings of Laboratory Services

Clinical laboratories are present in additional settings, including community clinics, ambulatory surgical centers, student health facilities, and pharmacies which, together, account for approximately 26% of all laboratories (see Table 2.4).¹⁶

In 2006, their estimated combined revenue was \$2.9 billion. Growth among these laboratories is slowing primarily because of lower overall revenues at the contract level and costs associated with CLIA regulatory requirements.^{1, 35, 52}

Table 2.4: Other types of laboratories by prevalence in the U.S., 2006

Type of Laboratory	Number	Percent of Total Laboratories	Total Annual Test Volume (million)	Waived Testing as Percentage of Total Annual Test Volume
Community Clinic	6,588	3.32%	75.9	28.7%
End Stage Renal Disease Dialysis Facility	4,099	2.07%	12.9	83.0%
Ambulatory Surgical Centers	4,023	2.03%	25.7	13.5%
Pharmacy	3,815	1.92%	73.3	99.9%
Ambulance	2,831	1.43%	3.0	73.5%
Ancillary Test Site in Health Care Facility	2,722	1.37%	67.7	36.9%
Other Practitioner	2,554	1.29%	29.2	11.9%
School/Student Health Facility	1,873	0.95%	5.5	42.3%
Hospice	1,872	0.94%	3.5	48.3%
Industrial	1,677	0.85%	2.3	67.2%
Rural Health Clinic	1,226	0.62%	3.9	47.6%
Mobile Laboratory	1,117	0.56%	5.0	58.6%
Interm. Care Facility, Mentally Retarded	985	0.50%	1.7	52.5%
Health Maintenance Organization	677	0.34%	100.7	4.3%
Health Fair	516	0.26%	13.0	7.0%
Federally Qualified Health Center	444	0.22%	1.4	52.7%
Blood Banks	375	0.19%	83.9	12.2%
Comprehensive Outpatient Rehab. Facility	272	0.14%	1.7	67.5%
Insurance	42	0.02%	5.4	0.8%
Tissue Bank/Repositories	36	0.02%	0.895	1.3%
Not Otherwise Specified	15,300	7.72%	267	25.3%

Source: CLIA update—December 2006, laboratories by type of facility. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006.

MARKET FOR LABORATORY TESTS

There is no definitive estimate of how many clinical laboratory tests are available. However, a large independent clinical laboratory currently lists over 4,000 tests on its testing menu.⁵³

According to the American Society for Clinical Laboratory Science (ASCLS), of the 1,162 tests reimbursed by Medicare, about 500 are performed regularly.⁵⁴

Laboratory tests are categorized by the following key areas:

- Anatomic pathology
 - Cytology
 - Surgical pathology
 - Oncology
 - Neuropathology
 - Immunohistochemistry
- Clinical pathology
 - Molecular pathology
 - Cytogenetics
 - Genetics
 - Histocompatibility
 - Microbiology
 - Immunology
 - Chemistry (including toxicology and drugs of abuse testing)
 - Hematology
 - Immunohematology
 - Radiobioassay¹⁴

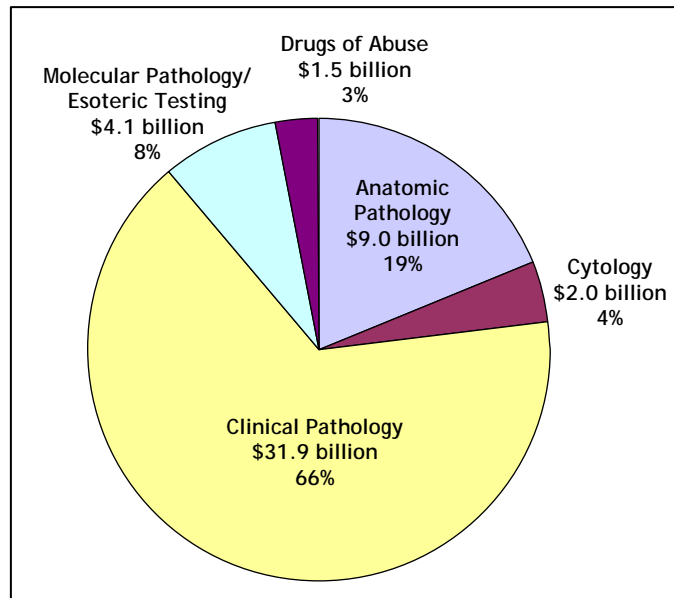
Most of the tests are performed at the request of a clinician, although patients and other consumers may order tests directly from the laboratory in some states. Discussion of the market for consumer direct access testing (DAT)ⁱ and over-the-counter (OTC) tests is provided subsequently in this chapter.

The market for clinical pathology is estimated to be \$31.9 billion in 2006, comprising nearly two-thirds of the industry (Figure 2.9).¹ Anatomic pathology and cytology are estimated to have markets valued at \$9 billion and \$2 billion, respectively. The market for molecular and other esoteric tests^j is about \$4.1 billion, and that for drugs of abuse testing is \$1.5 billion.

ⁱ DAT is known by a variety of other names, including consumer ordered tests, patient-directed tests, consumer driven tests, patient authorized tests, and consumer self-orders.^{55, 56}

^j The term “esoteric” refers to new molecular pathology tests and certain other relatively low volume tests. Most esoteric tests use molecular-based laboratory techniques.

Figure 2.9: Major Testing Segments in the U.S. Laboratory Industry, 2006

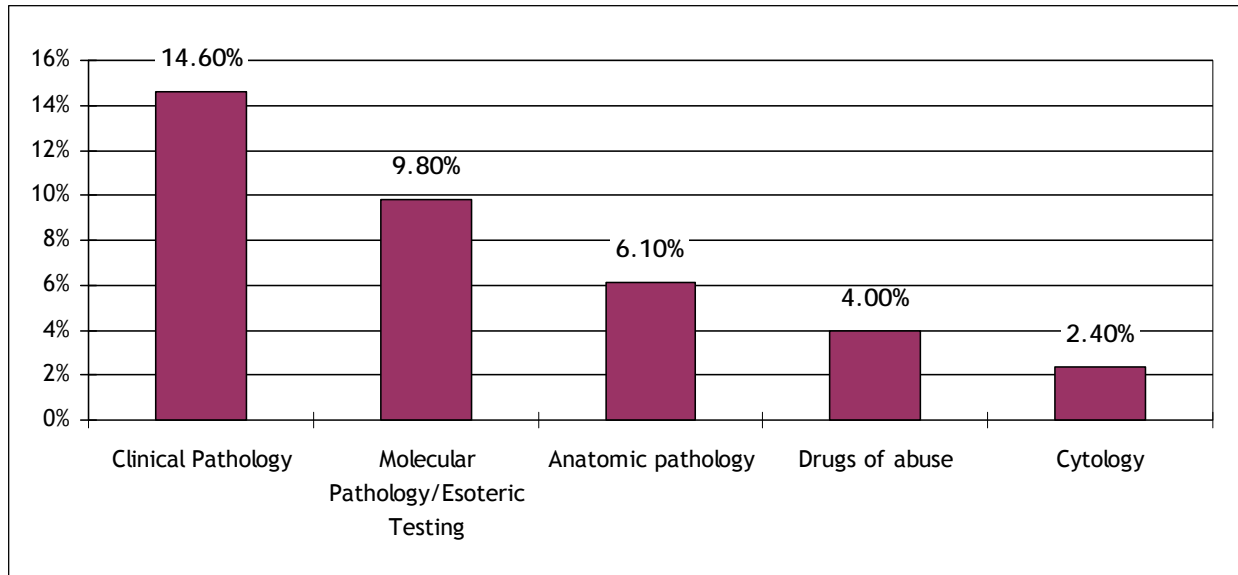


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2007. New York, NY: Washington G-2 Reports, 2007.

Figure 2.10 highlights the two-year average growth rate in each category. The market for all testing areas is expanding, except drugs of abuse testing. Growth in clinical pathology and molecular/esoteric testing is expected to average 11% in 2007. Contributing to the growth in molecular pathology testing are higher reimbursement rates, greater demand from both consumers and providers, and increases in the number of new predictive laboratory tests available.

Growth in anatomic pathology is expected to average 5% in 2007.¹ This growth is due mainly to changes in the burden of disease in the population, stakeholder interest in expanding methods of early detection to decrease health care costs, and technological innovation that has simplified testing techniques in areas such as flow cytometry and immunohistochemistry, allowing for more ubiquitous anatomic pathology testing in hospital and independent laboratories. The largest increase in test volumes is expected to occur in FISH and polymerase chain reaction (PCR)-based testing.⁵⁷

Figure 2.10: U.S. Laboratory Segment Annual Growth Rates, 2004 - 2006



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Market for Anatomic Pathology Testing

Anatomic pathology consists of the subspecialties of cytology, immunohistochemistry, neuropathology, dermatopathology, oral pathology, forensic pathology, autopsy pathology, and histology. Cytology refers to the diagnosis of cells from all systems and areas of the body.⁵⁸ Histology involves the study of tissues and cells under a microscope.⁵⁹ Immunohistochemistry involves use of antibodies to detect specific proteins that are expressed in tumors.^{k,60} Neuropathology is the branch of medicine dealing with diseases of nervous system tissue, specifically the brain and spinal cord.⁶¹ Dermatopathology is the study of diseases of the skin, including infectious, immunologic, degenerative, and neoplastic diseases.⁶² Oral pathology refers to the study of diseases affecting the oral and maxillofacial regions.⁶³ Forensic pathology concerns the examination of living or dead persons in order to provide an opinion on the cause, mechanism, and manner of disease, injury, or death.⁶⁴ Autopsy pathology refers specifically to the external and internal examination of the body after death.⁶⁵

Together, anatomic pathology and cytology account for about 23% of the laboratory industry by testing volume. Aside from cytology, market data for the other anatomic pathology testing areas are not available.

Three major privately-owned independent laboratories collected an estimated \$2 billion in anatomic pathology revenues in 2006.¹ Despite consolidation efforts among privately-owned independent laboratories, the anatomic pathology market remains relatively fragmented. More than 70% of the anatomic pathology market is occupied by thousands of pathology groups, including small and mid-sized private practices, independent laboratories, and hospitals.⁶⁶

^k Immunohistochemistry is considered anatomic pathology because it is conducted on biopsies and surgical specimens as opposed to bodily fluids (e.g., blood, urine).

According to CMS data, about 8,015 laboratories perform anatomic pathology tests, generating an annual volume of nearly 1.45 million tests.⁶⁷

Table 2.5 summarizes responses from 190 anatomic pathology laboratories to a survey regarding average annual testing volumes conducted in 2007. Respondents self-identified as belonging to one of four groups, three of which were hospital-related.⁵⁷ While average testing volumes in independent laboratories exceeds average testing volumes in some hospital-based laboratory arrangements for certain types of testing (e.g., surgical pathology accessions, immunohistochemistry), these results indicate that the majority of anatomic pathology testing is conducted in hospital laboratories. For example, 82% of liquid-based Pap smears and 86% of other molecular diagnostic tests are performed in hospital-related laboratories.

Table 2.5: Self-Reported Anatomic Pathology Testing Volumes by Type of Practice, 2007

	Hospital-Related Sites			Independent Lab ^d	Total Volume by Testing Type	% of Work Conducted in Hospital-Related Labs
	Hospital ^a	Pathology Practice Group ^b	Other ^c			
Surgical Pathology Accessions (All)	18,322	30,057	29,723	48,577	126,679	78.4%
- Biopsies	12,914	17,368	20,451	23,937	74,670	83.3%
- Immunohistochemistry	5,305	3,290	4,010	10,334	22,939	80.3%
Fluorescent In Situ Hybridization	469	215	86	1,331	2,101	72.4%
Cytopathology	15,380	18,592	19,208	34,181	87,361	80.0%
Liquid-based Pap Smears (All)	16,023	27,339	17,774	32,786	93,922	82.1%
- Thin-layer Automated Imaging of Pap Smears	9,540	13,530	10,308	22,476	55,854	79.3%
Other Molecular Diagnostic Tests	501	10	3,541	879	4,931	86.3%
Polymerase-Chain Reaction-Based Tests	926	2,162	1	3,106	6,195	73.7%
All Other Non-Surgical Pathology Accessions (e.g., electronic microscopy accessions) [±]	9,652	13,169	15,226	21,108	59,155	64.3%
Total Volume by Practice Type*	61,273	91,544	85,559	141,968	380,344	80.1%

^aRefers to pathologists who receive a salary from the hospital and conduct testing of specimens collected from hospital inpatients and outpatients

^bRefers to pathologists who have formed a private business group and who have contracted with a hospital to perform testing in that hospital's laboratory. These pathologists conduct inpatient, outpatient, and outreach testing. They bill insurance companies directly for the work they perform (professional component only); they maintain their own billing and revenue systems

^cRefers to pathologists who work in multihospital systems, integrated delivery systems, academic medical centers, or university hospitals

^dRefers to pathologists who work in an independent laboratory where the laboratory, testing equipment, and office space is not owned by a hospital system. These pathologists usually conduct testing on specimens collected in outpatient settings, but also

can function as reference laboratories for hospitals and other facilities. They bill insurance companies for both the technical and professional components of testing.

*Biopsies, immunohistochemistry, and thin-layer automated imaging of Pap smears were not included in calculation of total volume by type of practice because they are sub-categories of surgical pathology and liquid-based Pap smears, respectively. Volumes for these tests are included here to show breakdowns of specific tests.

†This category may include some molecular diagnostic testing (e.g., FISH, PCR-based testing) because some respondents may have included all molecular diagnostic testing in the “non-surgical pathology accessions” category rather than delineating these tests by specific category.

Source: Modified and reprinted with permission from Washington G-2 reports. Business strategies for anatomic pathology, including state of the market report, 2007. New York, NY: Washington G-2 Reports, 2007.

Anatomic pathologists/technologists in all settings are becoming more specialized.⁶⁸ Some laboratories and practice groups hire staff members with expertise in a particular organ system or testing method. Other groups hire individuals with doctoral degrees in specific areas, such as molecular biology, to research and develop new testing procedures.⁶⁹ To expand their business, these groups also are beginning to market specific tests or services directly to physicians and patients.⁷⁰

Cytology

Cytologic testing remains the gold standard in detection of many types of diseases, including common forms of cancer (e.g., uterine and cervical cancers, leukemia, lymphomas).⁷¹ In some instances, traditional cytologic tests are being replaced by newer technology. For example, an inexpensive point-of-care test to detect bladder cancer recently developed may be substituted for traditional laboratory-based cytologic testing.⁷²

The value of the cytology market is approximately \$2 billion.¹ From 2003 to 2006, cytological testing grew by 60%.⁶⁶ Although the cytology market has been undergoing some consolidation, it remains fragmented, with the majority of the market held by independent laboratories and hospitals.

A major contributor to the growth of cytology has been the nearly complete transition from traditional Pap smear tests to liquid-based thin-layer slide preparation testing methods for cervical cancer screening.⁷³ Whereas traditional Pap smear testing involves using a fixative to spray specimen cells onto a glass slide prior to sending them to a laboratory for analysis, the thin-layer testing method allows the specimen to be mixed into a vial of liquid preservative, which is then sent to the laboratory and made into slide samples, providing for cleaner and more uniform analysis.⁷⁴ In 2006, 92% of laboratories used thin-layer Pap test method to conduct cervical cancer screenings; however, by 2007, this number was projected to increase to 99%.^{1,75}

Thin-layer Pap smear tests are reimbursed approximately \$10 more than conventional tests, and increased use of thin-layer tests has contributed significantly to the growth in cytology-related revenue over the past several years.¹ From 1998 to 2005, revenue generated by gynecologic cytology testing has more than doubled, with revenues in 2005 exceeding \$1.38 billion.¹ More than 80% of the gynecologic cytology manufacturing market is dominated by two privately owned companies.

¹ Medicare reimbursed thin-layer tests at the same rate as traditional Pap smear tests until April 2001; Medicare's increase in reimbursement for thin-layer tests is believed to have accelerated acceptance of this form of testing.¹

Market for Molecular Pathology

Although molecular laboratory tests fall under the umbrella of clinical pathology, molecular testing techniques are increasingly applied in anatomic pathology. Thus, many experts are now discussing the blurring of the traditional lines between clinical and anatomic pathology. This discipline includes the categories of histocompatibility (e.g., assays to determine whether recipient and donor share antigens to ensure that a donated graft is accepted and remains functional); cytogenetics (e.g., analysis of amniotic fluid to detect fetal genetic abnormalities); hematopathology (e.g., tests to determine recipient genotype prior to bone marrow transplantation); infectious disease (e.g., HIV genotyping and determination of status of hepatitis B virus infection); inherited disease (e.g., cystic fibrosis carrier screening); and pharmacogenomics (e.g., genotyping to guide warfarin dosing).⁷⁶⁻⁷⁹

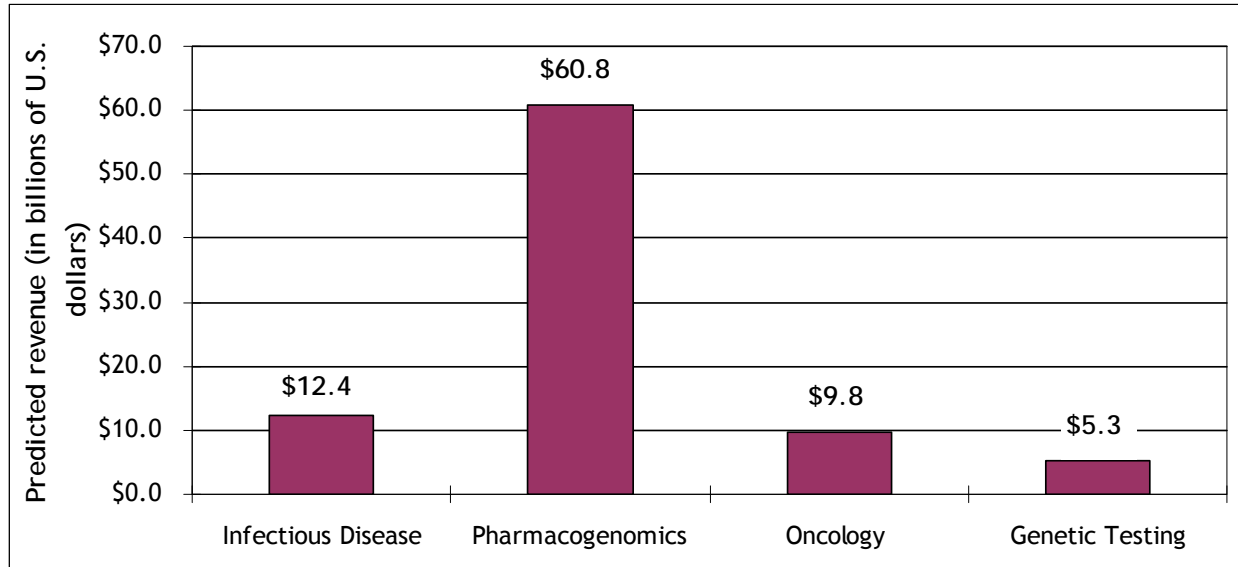
In 2007, the U.S. molecular diagnostic testing market was valued at approximately \$4.1 billion, representing the fastest-growing and most-profitable area of the clinical laboratory industry.⁸⁰ Market researchers anticipate continued growth in the molecular diagnostic market of approximately 19% per year over the next three years. The exact number of genetic tests available is not known, but an estimated 1,430 diseases are currently detectable using genetic testing (287 diseases are tested only in research settings).⁸¹

Key areas of growth include infectious disease testing, pharmacogenomics, genetic testing, and oncology testing. Figure 2.11 displays predicted revenues for each of these areas within the context of the worldwide molecular diagnostic market in 2016. By then, the U.S. is expected to generate nearly \$46.2 billion in revenues, half of the world market. Infectious disease testing is the largest area of the molecular diagnostic market, due to the high incidence of infectious disease and the relative ease with which genetic information required for identifying pathogens is obtained from bacterial and viral species.⁸² Pharmacogenomic, genetic, and chromosome testing represent the next largest areas of growth. For example, cytogenetic laboratory tests involve preparation of cells and isolation of chromosomes in order to identify chromosomal abnormalities (e.g., tests to detect the presence of fragile X syndrome, the most common inherited cause of mental impairment and the most common known genetic cause of autism). About 1.6 million cytogenetic tests are performed annually in 373 laboratories.⁶⁷

Molecular diagnostic testing is changing the practice of laboratory medicine. For example, laboratory testing is expected to have an important role in the growth of personalized and preventive medicine.⁸³ Molecular testing techniques are increasingly being applied to oncology and cardiology and tests to determine genetic expression and gene profiles, allowing clinicians to detect disease at much earlier stages. Although many molecular tests are currently still in the research stage, they are expected to become part of routine clinical practice over the next several years.

Laboratory experts predict that all neoplastic tissues will eventually be analyzed biochemically and morphologically.⁸⁴ Expression profiling, by which expression patterns of thousands of individual genes in a given cell or tissue sample can be discerned, may become standard practice alongside traditional histopathology.⁸⁵ If the historical line separating anatomic and clinical pathology continues to dissolve, pathology residency programs will likely need to adapt to emphasize training in both the morphologic and molecular basis of disease.⁸⁴

Figure 2.11: Predicted Average Revenue in 2016 for Segments of the International Molecular Diagnostic Market



Source: Molecular diagnostics: major world markets. New York, NY: Kalorama Information, 2007.

Techniques from molecular biology, identity testing, transplantation, and anatomic pathology are fueling many of the advances in molecular diagnostics.⁸⁶ For example, rapid molecular testing is now available using nucleic acid extraction techniques, allowing for more immediate initiation of therapy. Information derived from the sequencing of the human genome is enabling creation of molecular diagnostic tools that help to reveal the presence and roles of additional genes and gene products in complex diseases. Advances in innovative automated systems to support molecular diagnostic testing technologies also are improving laboratory practice by decreasing TATs, improving precision of quantitative results, and reducing costs (relative to manual testing).⁸⁷

Higher reimbursement rates for molecular tests are contributing to the accelerated growth in this area. According to a recent market analysis, the average charge for a non-molecular test is approximately \$30.39, compared to \$176.77 per molecular test.⁷³ Automation of molecular and genetic testing will likely affect the budgets and operating costs of laboratories performing these tests.

Market for Clinical Pathology Testing

Clinical pathology comprises the largest segment within laboratory testing; the market is currently valued at \$31.9 billion, or approximately 66% of the industry.¹

Waived Tests. According to CMS, waived testing accounts for approximately 11% of annual laboratory testing volume.⁶⁷ In 2006, annual volume of waived testing approached 700 million tests and generated annual revenue of \$1 billion. Approximately 75% of waived testing is conducted in laboratories certified to perform only waived or PPM testing, although about 17% is conducted by laboratories with a COA and about 8% by those with a COC (see Table 2.6).¹⁹

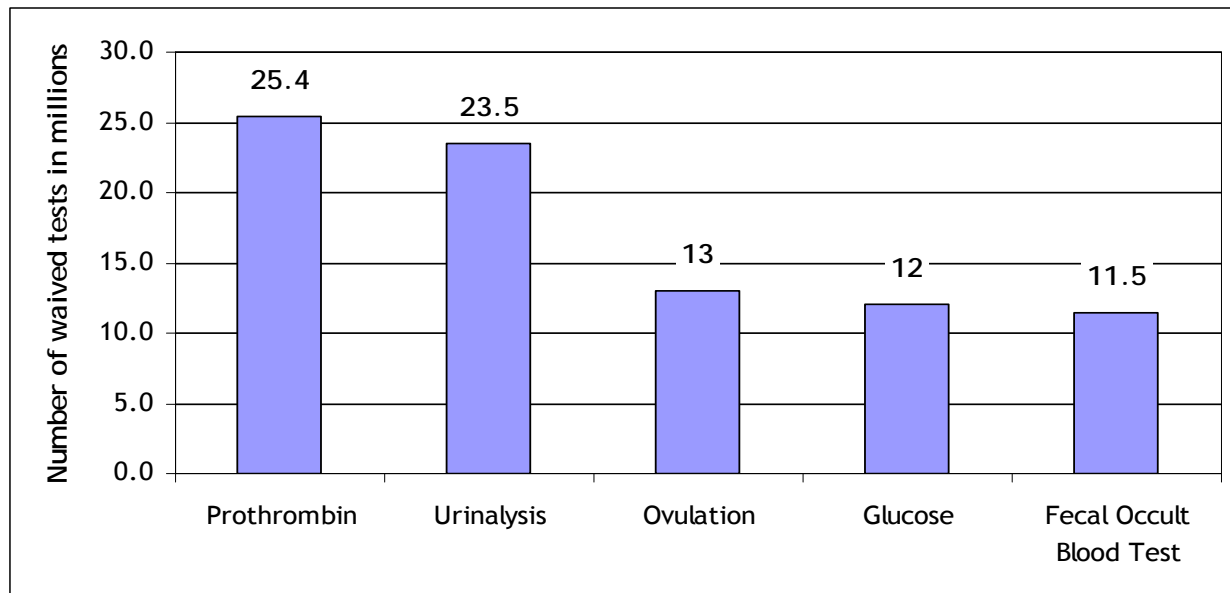
Table 2.6: Number of Waived and Non-Waived Tests Performed According to Laboratory Data Self-Reported to CMS, 2006

	Laboratories Certified to Perform only Waived or PPM Testing	Laboratories with Certificate of Accreditation	Laboratories with Certificate of Compliance	Total Number of Tests Performed
Number of <i>Waived</i> Tests Performed	523,797,097	121,240,212	54,890,056	699,927,365
Number of <i>Non-Waived</i> Tests Performed	Not applicable	4,614,509,645	921,013,600	5,535,523,245

Source: OSCAR/CLIA data base: Test volume information based on laboratory self-reporting on CMS-116. Zeller C, ed. Baltimore, MD: Centers for Medicare and Medicaid Services, March 2006.

According to OSCAR data obtained by Washington G-2 Reports, the highest-volume waived tests performed by all laboratories include those to evaluate prothrombin, urinalysis, ovulation, glucose, fecal occult blood test, and the lipid panel (Figure 2.12).¹ From 2000 to 2006, tests for 36 analytes (for which waived tests were not previously available) were granted CLIA waived status.⁸⁸ With new technology and simplification of testing techniques, the number of tests receiving waived status will continue to increase.

Figure 2.12: Five Highest Volume Waived Tests



Sources: Medicare part B physician/supplier national data CY 2005: Top 100 lab procedures. Baltimore, MD: Centers for Medicare and Medicaid Services, 2005. (Accessed November 10, 2007, at <http://www.cms.hhs.gov/MedicareFeeForSvcPartsAB/Downloads/LabServ05.pdf?agree=yes&next=Accept>.)

Terry M. Lab industry strategic outlook: Market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Moderate and High Complexity Tests. Although only 20% of laboratories are certified to perform moderate and high complexity tests, approximately 89% of laboratory testing volume is moderate or high complexity (non-waived) testing.¹⁹ In 2006, the volume of non-waived testing exceeded

5.5 billion (Table 2.6). The majority of non-waived testing is conducted in laboratories that have a certificate of accreditation.

As per CLIA regulations, CMS delineates non-waived clinical pathology laboratory tests into selected specialty areas. For clinical pathology, these areas include: chemistry, hematology, diagnostic immunology, microbiology, immunohematology, histocompatibility, and radiobioassay.⁸⁹ While the information provided here is based on data collected by CMS, CLIA specialties are not all inclusive of the menu of available clinical pathology laboratory tests. For example, CLIA does not include a separate specialty for genetic testing or toxicology. An overview of each CLIA specialty, including purpose, examples of specific tests, annual volume, and number of laboratories performing that type of test is displayed in Table 2.7.

Data reported by laboratories to CMS indicate that 62% of all non-waived tests performed are chemistry tests, which measure compounds and chemical reactions in the body and include routine chemistry, endocrinology, urinalysis, and toxicology tests.^{67,89} Commonly performed routine chemistry tests include measurements of total cholesterol, calcium, triglycerides, glucose, electrolytes, blood urea nitrogen, creatine, and prostate specific antigen (PSA). Examples of endocrinology tests include measurements of testosterone, thyroid-stimulating hormone, and progesterone; toxicology tests include measurements of acetaminophen, blood alcohol, digoxin, and lithium.

Accounting for 24% of all laboratory testing, hematology studies the blood, blood-producing organs, and cells of the body.^{67,90} Examples of hematological laboratory tests include measurements of red and white blood cells, differential blood counts, prothrombin time, and activated clotting time.⁸⁹

Diagnostic immunology, which involves measurement of the body's response to infection and inflammation, accounts for approximately 4.3% of testing.⁶⁷ Frequently ordered immunological tests include mononucleosis assays, antibody assays for viruses such as herpes and hepatitis, mycoplasma pneumoniae assays, and tests to detect rheumatoid arthritis.^{78,89}

Microbiological testing also comprises 4% of non-waived testing and refers to the detection, identification, and measurement of disease-causing microorganisms (e.g., viruses, bacteria, fungi, algae, parasites).^{67,90} For example, antigen assays detect streptococcal infection and culture assays detect and identify bacteria that cause urinary tract infection.⁸⁹

Immunohematology, or blood banking, involves the preparation of blood and blood components for transfusion and the selection of appropriate and compatible blood components for transfusion.⁹¹ Approximately 2.4% of moderate and high complexity testing falls into the category of immunohematology.⁶⁷ Common immunohematology tests are those that determine blood and Rh type and that screen and identify antibodies.⁸⁹

Smaller percentages of non-waived testing falls into the areas of radiobioassay (0.2%), histocompatibility (0.7%), and cytogenetics (0.03%).^{67,92} Radiobioassay tests determine the type, quantity, concentration, and location of radioactive material in the body (e.g., test of red cell volume, Schilling's test for B12 absorption).^{89,93} Histocompatibility tests assess the extent to which an organ donor and organ recipient share antigens and an organ can be successfully transplanted

(e.g., human leukocyte antigen typing to determine the proteins on white blood cells that make each person's tissue unique).⁷⁸

Table 2.7: Annual Testing Volume, and Number of Laboratories Performing Clinical Pathology Laboratory Testing According to CMS Laboratory Test Categorization

Clinical Area	Examples of Commonly Ordered Laboratory Tests	Approximate Annual Test Volume	Number of Laboratories Performing Tests
Chemistry	<ul style="list-style-type: none"> ▪ Cholesterol, total ▪ Uric acid ▪ Glucose (blood sugar) ▪ Ferritin ▪ Folate ▪ Blood alcohol ▪ Acetaminophen 	3.5 billion	25,755
Hematology	<ul style="list-style-type: none"> ▪ Red blood count ▪ White blood count ▪ Platelet count ▪ Hemoglobin ▪ Hematocrit 	1.4 billion	24,663
Diagnostic Immunology	<ul style="list-style-type: none"> ▪ Mononucleosis assays ▪ Rheumatoid arthritis ▪ Febrile agglutinins ▪ Human Immunodeficiency Virus ▪ Hepatitis or herpes antibody assays 	238 million	12,804
Microbiology	<ul style="list-style-type: none"> ▪ Streptococcal testing ▪ Bacterial cultures ▪ Gram stains 	225 million	20,056
Immunohematology	<ul style="list-style-type: none"> ▪ ABO blood type ▪ Rh(D) type ▪ Compatibility testing (cross-matching) ▪ Antibody screening 	131 million	6,956
Radiobioassay [‡]	<ul style="list-style-type: none"> ▪ Red cell volume ▪ Schilling's test 	10 million	611
Histocompatibility	<ul style="list-style-type: none"> ▪ Human leukocyte antigen typing (disease associated antigens) 	4.0 million	260

[‡]Radiobioassay testing may not always be considered part of the clinical laboratory and instead may be classified as a part of nuclear medicine.

Sources: Histocompatibility and immunogenetics terminology. Mt. Laurel, NJ: The American Society for Histocompatibility and Immunogenetics, 2007. (Accessed April 27, 2007, at <http://www.ashi-hla.org/>).

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OSCAR/CLIA data base: Test volume information based on laboratory self-reporting on CMS-116. Zeller C, ed. Baltimore, MD: Centers for Medicare and Medicaid Services, April 2007.

Market for Drugs of Abuse Testing

Drugs of abuse testing is used to determine the presence or absence of illegal drugs in an individual's body. Such testing is periodically conducted for designated workers in the public and private sectors.^m In the federal government, specific federal employees are required to undergo random drugs of abuse testing, including federal employees determined to be "testing-designated personnel" under the Federal Drug-Free Workplace Program, Department of Defense employees, Department of Transportation employees involved in aviation, railroads, mass transit, pipelines, and other transportation industries, and Nuclear Regulatory Commission employees and contractors.⁹⁴ In total, this includes about 16 million people. Under the Drug-Free Workplace Act of 1988, contractors and grantees of federal agencies must agree to provide drug-free workplaces prior to receiving a contract or grant; however, these programs do not require random drugs of abuse testing.⁹⁵ In the private sector, companies can voluntarily elect to implement drug-free workplace programs such as drug abuse prevention education.ⁿ

The drugs of abuse testing market was valued at approximately \$1.5 billion in 2006. About 33 million tests are conducted for employers annually. About 20% of these tests (approximately 7.5 million) are conducted for federal employees who are required to undergo drugs of abuse testing. A key factor contributing to market growth for drugs of abuse testing was the passage of the Drug-Free Workplace Act in 1988. The new rules required that all federal contractors and grantees ensure a drug-free workplace, prompting steep increases in drugs of abuse testing from 21% of employers in 1987 to 81% in 1996.

In order to conduct tests for federal agencies, laboratories must be certified by the government through the National Laboratory Certification Program of the Substance Abuse and Mental Health Services Administration (SAMHSA).^{o,96} While private companies can elect to use laboratories that are not certified by SAMHSA, many use these laboratories, considered to be the "gold standard" for drugs of abuse testing. Of the 45 laboratories currently certified to conduct federal workplace drugs of abuse testing, 11 are owned or operated by the two largest laboratory corporations.⁹⁷ In 2005, their combined revenue for drug testing was \$264 million, almost 28% of the market but a small percentage of their total revenue.¹ Other smaller companies may derive the majority of their revenue from drugs of abuse screening. Table 2.8 provides the estimated revenue for top 8 laboratories engaged in drugs of abuse testing in 2005.

^m Drugs of abuse testing also are an important part of forensic testing, although this topic is outside the scope of this report.

ⁿ Some states offer financial benefits to private companies that enact drug-free workplace programs. Some insurance companies provide lower rates to companies that have such programs in place.

^o SAMHSA oversees the Federal Drug-Free Workplace Program.

Table 2.8: Estimated 2005 Revenue at Top Eight Employee Drug Testing Laboratories

Company	Estimated Revenue 2005
Quest Diagnostics	\$165 million*
LabCorp	\$99 million*
First Advantage Enterprise Screening	\$72 million
Medtox	\$32 million
Psychmedics	\$21 million
Advanced Toxicology Network	\$19 million
Kroll Laboratory Specialists	\$18 million
Clinical Reference Lab	\$13 million
Total, top 8 companies	\$439 million

*Based on percentage of total revenue attributed to drug testing

Source: Reprinted with permission from Washington G-2 reports. Terry M. Lab industry strategic outlook: market trends and analysis 2007. New York, NY: Washington G-2 Reports, 2007.

Aside from federal employers, the number of employers requiring pre-employment drugs of abuse screening has decreased by 11% from 1999 to 2005.¹ Drugs of abuse testing of all employees on a regular basis has declined steadily from 1999 to 2004. Many employers have reported that drugs of abuse testing is not cost-effective, particularly when the actual number of positive test results is quite low. In 1999, the most current year for which data of this nature is available, the American Civil Liberties Union reported that, of the \$11.7 million (1990 dollars) spent by the federal government to screen 29,000 employees, only 153 tests were positive.⁹⁸

To decrease expenses, drugs of abuse testing for non-federal employees is increasingly being conducted in POLs, clinics, or on site in employer-based health departments or clinics using waived test kits.^P Kits sold over-the-counter through retailers (e.g., CVS, Wal-Mart) typically cost \$3 to \$5, compared to laboratory-performed tests, which cost \$25 to \$50.¹ Although OTC testing of drugs of abuse may be less accurate and reliable than laboratory-performed tests, this shift in testing location has resulted in the closing of many drug testing laboratories. From 1998 to 2007, the number of SAMHSA-certified laboratories decreased from 71 to 45, a 36% drop.^{1,97} While many states do not have special requirements to govern employers who perform their own drugs of abuse testing, some states do require that all positive test results be confirmed in a SAMHSA-certified laboratory.⁹⁹

Market for Consumer-Directed Tests

An increase in the amount of information available to the public via the Internet and news media attention to personal health issues have enhanced consumer interest in understanding, directing, and managing their health care.^{84,100} The increasing number of Americans who are uninsured or underinsured may be contributing as well, to the extent that they seek personal health information outside of the health care system. There is now a substantial market for health care services and products that support consumers in their self-care associated with prevention and disease management. Two chief avenues for consumers to engage in self-directed laboratory testing are DAT at an established laboratory and OTC tests.

^P Between 2000 and 2006, FDA approved 35 waived tests, 5 specifically for drug testing.

Direct Access Testing. Consumers have demonstrated strong interest in the ability to order laboratory tests and obtain results independently of a health care provider.¹⁰¹ Typically, DAT services are purchased out-of-pocket by the consumer without physician consultation.⁵⁵ A major concern regarding most DAT is that, in the absence of clinician prescribing and test interpretation, consumers are largely responsible for interpreting DAT laboratory results and may only follow up with their clinician if they deem it necessary.

Since CLIA or other federal regulations do not address DAT, its governance falls under state law.⁵⁵ Some states prohibit hospital laboratories from performing DAT, while others prohibit hospitals only from conducting DAT for inpatients. In 2007, 13 states prohibited DAT completely and 12 states permitted DAT with specific limitations.¹⁰² The remaining 25 states and the District of Columbia allow DAT either because statutes explicitly provided for it or there is no law against it. In 2004, 10-15% of hospital and commercial clinical laboratories offered some form of DAT.¹⁰³

Consumer access to DAT varies based on the type of test and geographic location. Internet websites, telephone services, freestanding stores, hospital and commercial laboratory facilities, and pharmacies are currently the primary methods of access. While many DAT laboratories offer only simple tests, other laboratories offer more complex tests. Examples of tests commonly ordered via DAT services include those that measure complete blood counts, cholesterol levels, throat and urine infection, diabetes, HIV antibody tests, and blood type.⁵⁶

Another factor calling attention to DAT is direct-to-consumer advertising of laboratory tests, specifically genetic tests. For example, a provider of clinical BRCA1/2 tests, for detecting genetic mutations associated with predisposition for inherited breast and ovarian cancer, directly marketed these tests to consumers over a 6-month period, marking the first time a genetic test was marketed to the public.¹⁵ Providers in the pilot cities reported ordering more tests and reported an increase in the number of patients who asked about testing, asked for genetic counseling referrals to consider testing, and requested testing. The chapter on regulation of laboratory medicine in this report provides a more detailed discussion of direct-to-consumer advertising of genetic testing.

Over-the-Counter Tests. Consumers can purchase laboratory kits for certain types of tests and perform the tests themselves at home.¹⁰⁴ These tests are purchased OTC at drugstores and supermarkets as well as on the Internet. OTC laboratory kits available for home use include (but are not limited to) ovulation detection tests, pregnancy tests, and certain tests that measure and monitor cholesterol, glucose, fecal occult blood, and urinary tract infections. The average price of individual tests varies, ranging from \$20 for ovulation detection and cholesterol tests to \$30-\$100 for instruments that monitor glucose levels. Currently, FDA has approved more than 800 laboratory tests that can be sold OTC; more than 160 tests were approved in 2007 alone.¹⁰⁵

Laboratory tests performed at home by the consumer can offer certain advantages. They provide a means by which individuals can monitor a disease that has already been detected by a physician.¹⁰⁴ Secondly, home testing also allows individuals to detect certain conditions in the privacy of their home. However, laboratory tests performed at home also pose the risk of inaccurate test results or incorrect interpretation of results, and failure to receive medical advice and attention if needed.

Research examining the accuracy of home-use tests versus tests performed in a central laboratory show mixed results. For example, a study of 111 patients with type 1 and 2 adult diabetes found

that, compared to blood glucose values obtained from a calibrated hand-held glucose monitor, 53% of blood glucose measurements using home testing kits were within 10% of the control value, 84% were within 20% of the control value, and 16% varied by 20% or more from the control value.¹⁰⁶ A 2006 review of available evidence on self-monitoring using home-use glucose meters found that, while these devices are far more accurate than the earlier approach of matching colors, they are not as accurate as those derived from laboratory testing. Even so, if used properly, they give an acceptably accurate reflection of immediate plasma glucose levels. The authors noted that, in the relatively near term, self-monitoring of blood glucose could be replaced gradually by continuous glucose monitoring.¹⁰⁷

RESEARCH-SUPPORT TESTING

Research-support testing is often used in clinical research trials. Although research laboratories devoted to clinical trial support are exempt from CLIA requirements, they must comply with FDA regulations and inspections governing the studies.

In recent years, the pharmaceutical industry has outsourced the management and design of clinical trials to contract research organizations (CROs).¹⁰⁸ The CRO industry has grown with the expansion of clinical trials. Enrollment of individuals in clinical trials also increased from 7 million in 1992 to 20 million in 2001. In 2006, the market for Phase I-IV studies^q by CROs was valued at approximately \$8.5 billion; 8 firms hold 63% of the market.¹¹⁰ The largest providers of phase I-IV and central laboratory services in the CRO industry are Quintiles, Pharmaceutical Product Development, Inc., and Covance. Together, these three account for 37% of the CRO market. CROs can be involved in many different aspects of clinical trials, including preclinical safety analysis, study design, clinical trial management, laboratory services, statistical analysis, and regulatory services.¹⁰⁸ There are approximately 1,500 CROs in existence today.¹¹¹ Roughly 20 CROs conduct business on a global basis, while the remaining ones conduct clinical trials in smaller regions.

While there are no reliable figures, approximately half of CROs in business today operate their own laboratories.¹¹¹ Many of these laboratories tend to be small, focusing solely on either basic or esoteric tests. The number of CROs offering laboratory services has increased as drug and medical device developers have demanded that CROs play a larger role in all phases of research.¹¹²

Covance reports that it has increased its volume of laboratory testing by more than 40% during the last two years. As part of this expansion, the company implemented a global automated specimen collection kit production line in which barcoded testing kits are assembled and sent to clinicians to simplify specimen collection and identification from research subjects. This method of production also enables monitoring each step involved in kit production, thereby achieving greater process control.^{111, 113}

Anecdotal evidence from industry experts suggests a synergistic relationship between larger and smaller CROs in regard to laboratory services and business markets. For instance, larger CROs might use the framework and relationships established by smaller, "niche" CROs to gain entry to

^q Clinical trials of most pharmaceuticals and biologicals and some medical devices are conducted in phases.¹⁰⁹ For most experimental products, Phase I and II trials involve determination of treatment safety, dosage, and side effects; Phase III trials involve confirmation of efficacy and side effects and allow comparison to commonly used treatments. Phase IV trials are post-marketing studies to obtain additional information about risks, benefits, and optimal use.

the clinical research market in a foreign country. Smaller CROs, particularly those that do not house their own clinical laboratory services, may use the laboratories of larger CROs to facilitate their own clinical research.¹¹¹

CONCLUSIONS

The revenue, spending, and test volume of the U.S. clinical laboratory testing market has grown steadily over the past decade. Market expansion is attributed to changes in population demographics and burden of disease; scientific, medical, and technological advancements driving innovative research and development; and increased consumer awareness of and demand for high quality, safe health care.

- According to CMS, nearly 6.8 billion laboratory tests are performed annually in the U.S., with projected revenues of \$52 billion in 2007.
 - Clinical pathology testing comprises 66% of all laboratory tests and \$32 billion in revenue
 - Anatomic pathology and cytology account for 23% and \$11 billion in revenue
 - Molecular and esoteric testing account for 8% and \$4 billion in revenue
 - Drugs of abuse testing accounts for 3% and \$1.5 billion in revenue
- Today, over 4,000 thousand laboratory tests are currently available for clinical use. Of the 1,162 tests that are reimbursed by Medicare, about 500 are performed regularly. Medicare covers genetic tests only in a very limited capacity; most are not eligible for coverage unless they are indicated for symptomatic patients or are used to determine how a patient will respond to particular therapies.
- The number of genetic tests available is growing, although many of these tests are only used in research settings. Specifically, an estimated 1,430 diseases are currently detectable using genetic testing. Of these, 287 diseases are tested only in research settings.
- The number of CLIA-certified laboratories grew by 28% from 1993 to 2006, and exceeded 200,000 in 2007. POLs represent the largest number of clinical laboratories in this sector (106,190 or 54%); approximately 80% are certified to perform only waived and/or provider-performed microscopy tests including urinalysis, fecal occult blood, urine pregnancy, rapid streptococcal, and glucose tests.
- Hospital-based laboratories account for the largest proportion of total testing volume (55%) and generate the highest proportion of total testing revenue (54%), projected at \$28.4 billion for 2007. From 1999-2006, the average annual growth rates of both test volume and revenue were approximately 6 to 7%. In 2006, privately-owned laboratories generated revenues of \$15.5 billion (32% of total revenue), performing mostly routine, high-volume tests and molecular/esoteric tests.
- Consumer-directed testing in the form of DAT and OTC tests is a key area for current and future market growth. In 2004, 10-15% of hospital and commercial clinical laboratories offered some form of DAT.

Gaps, Needs, and Challenges:

- Publicly available information about the economic status and quality of the laboratory medicine sector is limited. The main sources currently available are CMS' OSCAR database, *ad hoc* surveys, and commercial market reports used for investment purposes. As a group, these leave certain gaps in covering the laboratory market, including precise figures of market revenues, spending, test volume, and laboratory testing trends. As a result, estimates about these facets and other descriptors are likely to be incomplete and imprecise. This lack of data inhibits the ability of researchers, regulators, payers, providers, and other stakeholders to adequately describe, anticipate the direction of, and influence this key health care sector. Better data sources would support improved assessment of the value of laboratory medicine, workforce development, growth and directions of test use, financing, quality improvement, and organizational and strategic planning.
- POLs are undergoing a major shift toward performing primarily waived testing. This shift is attributable to the growing number of FDA-approved waived tests available, industry's targeted marketing of waived tests to POLs, higher costs associated with workforce training, and other expenses required to comply with CLIA regulations for moderate and high complexity testing. The effect on quality of patient care of the shift to waived testing is unclear and may require further study.
- As consumer-driven testing increases, laboratories should be prepared to assume a greater advisory role to individuals seeking DAT and using OTC tests. Consumer demand for DAT is already creating incentives for laboratories to provide additional services. For instance, some laboratories offer consumers the opportunity to consult with a medical doctor via e-mail prior to ordering tests and to receive test results via e-mail. In addition, for all tests, laboratories can develop consumer-friendly, easily understandable laboratory reports, written interpretations, and related support to promote more informed self care by consumers, patient safety, and quality of care.

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CHAPTER III

LABORATORY MEDICINE WORKFORCE

The laboratory medicine workforce plays a vital role in the health care system, managing and applying evidence-based, scientific testing techniques to support patient care and protect against public health threats.¹ However, there is growing concern regarding a significant shortage in the number of laboratory professionals entering the workforce. The shortage could become pronounced soon with the forthcoming retirement of many laboratorians. At the same time, the demand for laboratory services continues to increase given such factors as the aging of the population, growing prevalence of chronic diseases, and availability of new testing methods. Innovative technologies also are changing the practice of laboratory medicine and, in turn, the educational requirements and staff qualifications needed to provide quality testing services.

This chapter provides an overview of the professionals in the laboratory medicine workforce, including their day-to-day responsibilities, demographic characteristics, vacancy rates, and wages. The chapter also addresses the status of educational programs for each professional group, including specialty education programs, changes in curriculum, and data on program enrollees and graduates. Lastly, this chapter discusses licensing and certification at the federal and state level.

TYPES OF PROFESSIONALS

Clinical laboratories typically are staffed with a medical team comprising pathologists, doctoral-level laboratory scientists, laboratory technologists and technicians, and phlebotomists. In addition to pathologists, personnel in anatomic pathology laboratories include histotechnologists/histotechnicians, cytotechnologists, and pathologists' assistants. POLs are typically staffed by medical assistants and/or laboratory technologists and technicians. Many of these professionals acquire additional training as a specialist within a subdiscipline of clinical laboratory testing.² While there can be overlap in some of their tasks, their contributions and responsibilities differ in certain important ways.

Pathologists and Doctoral-Level Laboratory Scientists

Pathologists and doctoral scientists frequently operate at the more senior levels in clinical laboratories. Often they serve as directors of clinical laboratories, responsible for oversight of staff, testing processes, quality control procedures, quality of laboratory care for patients, and other managerial functions. Pathologists are licensed medical doctors who have graduated from an allopathic or osteopathic school of medicine. They examine samples, interpret results of laboratory tests, ensure the accuracy of laboratory tests, and consult with clinicians.³ There is growing recognition of the vital roles of pathologists and doctoral-level laboratory scientists in the delivery of patient care by consulting with clinicians on ordering laboratory tests and interpreting the results.⁴ In most cases, pathologists and doctoral scientists can interpret and sign off on laboratory test results.^{a,5}

^a Some health care payers will not pay for laboratory test interpretation that is not conducted by a pathologist; in these cases, pathologists must interpret and sign off on laboratory tests. Some hospitals also require pathologist approval.⁵

Pathologists in all branches of laboratory medicine (i.e., anatomic pathology, clinical pathology, and interdisciplinary subjects) tend to specialize in and practice specific clinical disciplines, as outlined in Box 3.1. For pathologists and doctoral-level laboratory scientists, pathology-related subspecialties in which certification is available include: immunohematology and transfusion medicine, chemical pathology, cytopathology, dermatopathology, forensic pathology, hematology, histocompatibility, immunology, microbiology, molecular diagnostics, molecular genetic pathology, neuropathology, oral pathology, and pediatric pathology.⁶

Box 3.1: Certifications Available for Anatomic, Clinical, and Molecular Pathology Specialties

Clinical Pathology	Anatomic Pathology
Chemical Pathology (P, DLLS, T/S) Hematology (P, DLLS, T/S) Immunology (DLLS) Microbiology (P, DLLS, T/S) Histocompatibility* (P, DLLS) Immunohematology and Transfusion Medicine (P, T/S) - Hemapheresis** (T/S) - Apheresis** (T) Phlebotomy (T) Virology (T/S)	Cytopathology (P, T/S) Neuropathology (P) Dermatopathology (P) Oral Pathology (P) Forensic Pathology (P) Histology (T/S, T) Pediatric Pathology‡ (P)
	Molecular Pathology
	Molecular Genetic Pathology (P, T/S) Cytogenetics (T/S) Molecular Diagnostics (DLLS)

P= Certification available for pathologists

DLLS= Certification available for doctoral-level laboratory scientists

T/S= Certification available for technologists/scientists

T= Certification available for technicians

‡Pediatric pathology can consist of one or both of anatomic and clinical pathology.

* Pathologists can become certified as histocompatibility laboratory directors through the American Board of Histocompatibility and Immunogenetics.

**Specialists in hemapheresis have knowledge of all aspects of donor and therapeutic procedures. They have managerial responsibilities and make clinical and therapeutic decisions. Apheresis technicians work in donor and therapeutic settings and perform basic and intermediate apheresis procedures; they do not have managerial responsibilities and are not generally involved in clinical and therapeutic decision-making.⁷

Sources: About physician specialties: pathology. Evanston, IL: American Board of Medical Specialties, 2007.

Clinical Laboratory Improvement Amendments of 1988 (CLIA) application for certification. Baltimore, MD: Centers for Medicare and Medicaid Services, 2007.

Candidate handbook. Lenexa, KS: American Board of Histocompatibility and Immunogenetics, 2008. (Accessed April 28, 2008, at <http://www.ashi-hla.org/abhi/ABHI-handbook.pdf>.)

Reference resources and publications. Northfield, IL: College of American Pathologists, 2007. (Accessed May 2, 2007, at http://www.cap.org/apps/cap.portal?_nfpb=true&_pageLabel=reference.)

Doctoral-level laboratory scientists have earned advanced degrees in such laboratory-related fields as clinical chemistry, immunology, genetics, or microbiology; some have also completed postgraduate fellowships. They are often responsible for establishing new laboratory tests, interpreting test results, and ensuring accurate and appropriate test outcomes.⁸ Doctoral-level laboratory scientists can serve as laboratory directors, with responsibility for supervising the laboratory's technical and scientific functions.^{9,10} With greater automation of microbiological laboratory testing, doctoral-level laboratory scientists are shifting to emerging areas of laboratory testing involving genetics and pharmacogenomics.

Technologists/Scientists and Technicians

These laboratorians represent the two largest groups of laboratory professionals and can be involved in many aspects of laboratory specimen collection, preparation, and testing, depending on the nature of the test and their qualifications.

Each group is referred to by interchangeable titles by professional organizations, educational programs, and other clinical laboratory professionals:

- Medical technologists/clinical laboratory scientists (MT/CLSs)
- Medical laboratory technicians/clinical laboratory technicians (MLT/CLTs)

The largest certifier of laboratorians, the American Society for Clinical Pathology (ASCP), uses the titles of MT and MLT, whereas another certifier, the National Credentialing Agency for Laboratory Personnel (NCA), uses CLS/CLT. In 2005, ASCP and NCA began discussing the formation of one credentialing agency for laboratory personnel and unifying professional titles.^{11,12} Discussions are ongoing.

In order to minimize use of abbreviations and simplify terminology for this report, MT/CLSs will be referred to as *technologists/scientists* and MLT/CLTs as *technicians*. Unless otherwise noted, use of these personnel titles includes individuals that have received general certification and those that have received subspecialty certification.

Technologists/Scientists

Technologists/scientists have earned a bachelor's degree from an accredited college or university and have completed an accredited education program specific to medical technology or have met the education requirements and have obtained the laboratory experience defined by a certifying agency.^{13,14} Their training allows them to conduct laboratory tests on tissues, blood, and other bodily fluids and perform a range of complex chemical, biological, hematological, and immunologic tests.¹⁵ In addition, they may evaluate and confirm the accuracy of test results, report laboratory findings to pathologists and other physicians, and develop and alter test procedures.^{15,16} Technologists/scientists often advance to supervisory and managerial/administrative positions in which they provide day-to-day management of laboratory operations.

Technologists/scientists can pursue additional education to become certified in the specific areas of laboratory medicine noted in the section on certification, below. They may receive specialty certification in blood banking, chemistry, cytogenetics, cytology, hematology,

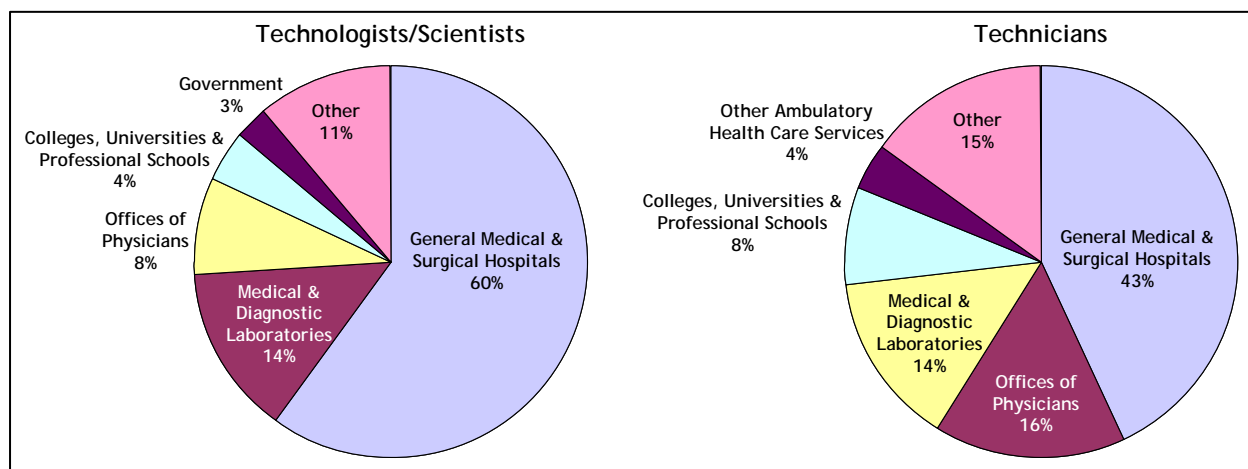
immunohematology, hemapheresis, histology, laboratory safety, microbiology, molecular pathology, and virology.^{13,14} About 60% of technologists/scientists work in general medical and surgical hospitals, followed by 14% that work in independent laboratories, and 8% in physician offices, among other settings (see Figure 3.1).¹⁷

Technicians

Technicians perform less complex tasks under the supervision of a technologist/scientist. They may prepare samples, operate automated analyzers, and perform manual laboratory tests in the areas of blood banking, chemistry, hematology, immunology, and microbiology.¹⁵ Technicians usually have an associate's degree from an accredited college or university, with training from an accredited laboratory technician education program or the equivalent.^{13,14} Technicians can pursue additional education to become certified as a technologist/scientist.^{13,14}

About 43% of technicians are employed in general medical and surgical hospital settings, 16% in physician offices, and 14% in independent laboratories (Figure 3.1).¹⁸

Figure 3.1: Distribution of Settings of Work for Technologists/Scientists and Technicians



Sources: Occupational employment and wages, May 2006; Medical and clinical laboratory technologists. Washington, DC: Bureau of Labor Statistics, 2007. <http://www.bls.gov/oes/current/oes292011.htm>

Occupational employment and wages, May 2006; Medical and clinical laboratory technicians. Washington, DC: Bureau of Labor Statistics, 2007. <http://www.bls.gov/oes/current/oes292012.htm>

Pathologists' Assistants

Through special training, individuals may become pathologists' assistants, who are often the first staff to look at an anatomic laboratory sample, provide the pathologist with a description of the sample, and assist in determining whether further analysis is required.¹⁹ Pathologists' assistants perform a variety of tasks and are primarily responsible for gross examination of surgical pathology specimens and conducting autopsies.²⁰ Prior to January 1, 2008, pathways to becoming a certified pathologist's assistant included earning a bachelor's degree and completing an accredited pathologists' assistant program or completing three years full-time experience as a pathologists' assistant under the supervision of a pathologist.¹⁹ This on-the-job training route has been discontinued; all certified pathologists' assistants must now complete a formal training program in order to qualify for certification.

Histotechnologists/Histotechnicians

Histotechnologists (HTLs) and histotechnicians (HTs) work in anatomic pathology laboratories to prepare tissue for microscopic examination by a pathologist.²¹ HTLs have advanced training in understanding how and why specimens are collected and processed. They are responsible for solving technical and instrumental problems that may arise in the laboratory, understanding the reasons for unusual test results, and evaluating new laboratory techniques and procedures. In order to qualify for certification as an HTL, individuals must have a bachelor's degree and must complete an accredited HTL program or an associate degree and one year full time experience in a histopathology laboratory.^{13, 22}

Cytotechnologists

Cytotechnologists are responsible for the microscopic examination of cell samples to detect signs of cancer and other diseases.²³ Cytotechnologists specifically analyze cell changes, both in the nucleus and cytoplasm, and compare these changes to normal cells from the same site. When findings for certain specimens are normal, cytotechnologists can issue the final laboratory report; when abnormal cells are detected, cytotechnologists work with pathologists to determine the final diagnosis. Individuals must have a bachelor's degree and complete an accredited cytotechnology educational program in order to become certified.²⁴

Medical Assistants

Approximately 62% of medical assistants are employed in POLs.²⁵ In this setting, medical assistants can be responsible for drawing blood and preparing laboratory specimens and performing basic laboratory tests.²⁶ While some medical assistants receive on-the-job training, this is becoming less frequent, and medical assistants increasingly complete formal educational programs that include clinical and academic training in areas such as medical terminology, laboratory techniques, clinical and diagnostic procedures, and patient relations.²⁵ Medical assistant educational programs must receive accreditation from designated agencies; graduates of these programs can apply for certification by organizations such as the American Association of Medical Assistants.

WORKFORCE DEMOGRAPHICS

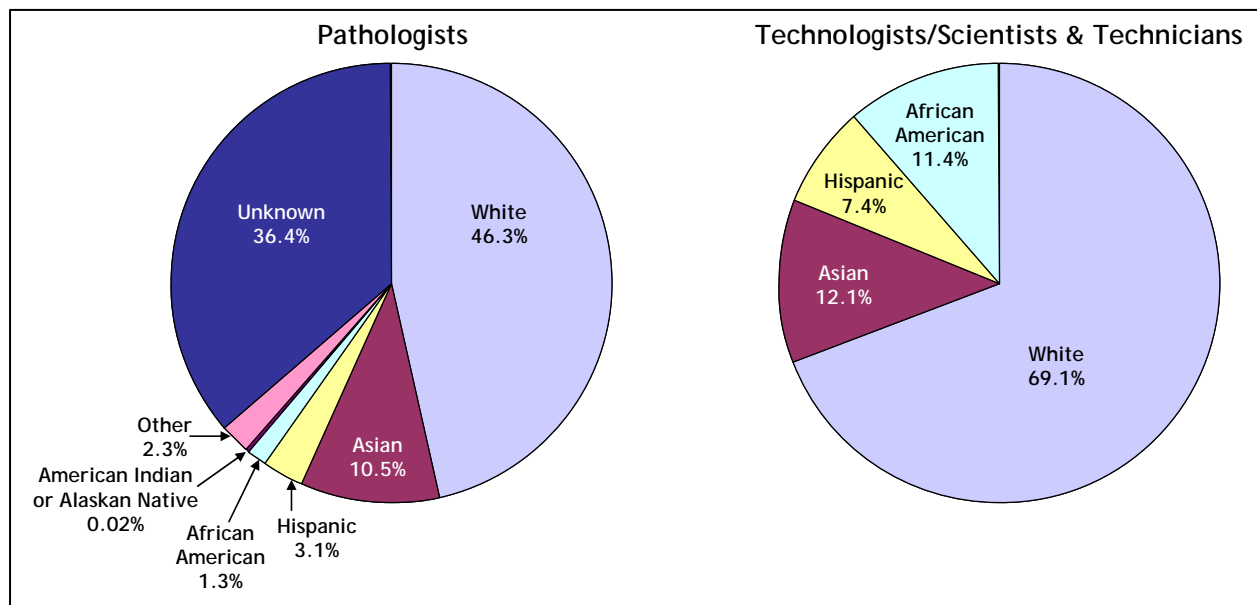
Pathologists and Doctoral-Level Laboratory Scientists

In 2005, there were an estimated 19,339 clinical and anatomic pathologists in the U.S.²⁷ Of these, 2,533 were residents and fellows in either discipline. According to the Intersociety Committee on Pathology Information, 80% of pathologists work in community practice, 15% work in academic practice and medical school administration, 3% work in industry, and 1% hold government, public health, and regulatory positions.²⁸ Data from 2006 show that slightly more than half of clinical and anatomic pathology residents and fellows were female and 34% were graduates of non-U.S. medical schools.⁶ While the percentage of female residents remained the same relative to 2005, approximately 37% of residents were graduates of non-U.S. medical schools in 2005. About 32% of full-time physician faculty members in clinical and anatomical pathology were female in 2006, compared to 31% in 2005.

According to the AMA, the pathologist workforce tends to be largely white (46% in 2005),²⁷ with 11% Asian, 3% Hispanic, 1.3% African American, 0.02% American Indian or Alaskan Native, and 2% identified as other; race/ethnicity was not identified by 36% of respondents. Figure 3.2 compares race/ethnicity data for pathologists, technologists/scientists, and technicians. These percentages are fairly representative of the ethnic and racial composition of the physician workforce as a whole. The geographic concentration of clinical and anatomic pathologists is fairly evenly dispersed throughout the U.S. In 2005, approximately 24% of the workforce was concentrated in the northeastern U.S., 22% were in the north central U.S., 34% were located in the southern U.S., and 19% were in the western U.S.²⁹

Demographic data for doctoral-level professionals in the laboratory medicine workforce are not available, though some rough inferences can be made from the profile of students receiving doctoral degrees in the life and physical sciences. In 2003, 52% of students awarded a doctoral degree in the life sciences were male, as were 72% of students receiving doctoral degrees in the physical sciences.^{30, 31} More than 80% of life and physical science doctoral degree recipients identified themselves as white, non-Hispanic. However, these percentages are shifting. The percentage of women awarded degrees in the life and physical sciences has been increasing over the past several years.

Figure 3.2: Comparison of Racial and Ethnic composition of Laboratorians, 2005



Sources: Physician characteristics and distribution in the U.S., 2007 edition. Chicago, IL: American Medical Association, 2007. Employed civilians by occupation, sex, race, and Hispanic origin: 2005. Washington, DC: U.S. Census Bureau, 2005. <http://www.census.gov/compendia/statab/tables/07s0602.xls>

Technologists/Scientists and Technicians

The technologist/scientist and technician workforce also has a female majority and is more representative of the racial/ethnic makeup of the U.S. population.¹ In 2006, there were an estimated 160,760 technologists/scientists and 144,710 technicians employed in the U.S.^{17, 18} Of these professionals, 74% were female.³² The racial/ethnicity distribution of the combined laboratorian

groups was 69% white, 12% Asian, 11% African American, and 8% Hispanic (Figure 3.2). In 2002, the last year in which such data is available, the median age of these laboratorians was 41.¹

The geographical distribution of technologists/scientists and technicians varies across the U.S. The Bureau of Labor Statistics defines workforce concentration as the number of people employed in a specific profession divided by the total number of people employed in all sectors in a defined geographic area. Concentrations also vary by urban, suburban, and rural status, and may not reflect the state concentrations listed above.

Based on data from multiple sources, the geographic distribution of these laboratorians is approximately as follows:

- The five states with the highest workforce concentration of technologists/scientists are Massachusetts, South Dakota, Louisiana, Nebraska, and Pennsylvania.¹⁷ About 58% of technologists/scientists are employed in an urban environment, 24% work in suburban areas, and 18% are employed in a rural location.³³
- The five states with the highest concentrations of technicians are Massachusetts, Pennsylvania, Tennessee, Kansas, and Indiana.¹⁸

VACANCY RATES

There is significant concern across the laboratory medicine sector about the growing shortage of clinical laboratory workers, which is expected to worsen over the next decade, particularly for technologist/scientist and technician positions.¹ Several factors are cited as contributing to this shortage: the pending retirement of many members of the workforce, competing career opportunities, and difficulty recruiting and retaining staff.^{1,34} The effects of technological advancement on the workforce appear to be mixed. While greater automation can decrease the need for personnel in the laboratory and enable non-laboratory personnel to perform tests, operating more advanced laboratory equipment can require more highly-trained technologists/scientists and technicians. These effects may shift the skill sets required for laboratory personnel at all levels.¹⁵

Pathologists and Doctoral-Level Laboratory Scientists

Currently available data do not indicate a shortage of pathologists.³⁵ However, virtually every academic department in the U.S. is reported to have a vacancy in pathology.²⁸ According to the ASCP's 2006 Resident Council Fellowship and Job Market Survey, 85% of respondents in their final year of residency or fellowship who had applied for a job had at least one offer of employment, an increase of 10% from the 2005 survey.³⁶ The remaining 15% are reported to have taken fellowship positions. Of those applying to pathology fellowship positions, 88% received at least one offer, a decrease from the 97% of applicants who were offered at least one fellowship in 2005.^b

Data on vacancies in doctoral-level laboratory scientists is not available, but anecdotal evidence from the American Board of Clinical Chemistry (ABCC) suggests that the number of individuals certified by the board each year has been decreasing over the past several years.³⁷

^b The decrease in the percentage of fellowship applicants who were awarded at least one fellowship is attributed to the increasing number of pathology residents applying for fellowships.³⁶

Other Laboratory Personnel

Vacancies for technologists/scientists and technicians, especially at the phlebotomist and cytotechnologist levels, are more extensive than for pathologists and doctoral-level laboratory scientists. The ASCP Board of Registry has been collecting information on vacancy rates on a biannual basis since 1988.¹ Their 2005 survey of wages and vacancies (Table 3.1) showed that vacancy rates for both were highest prior to 2002 before dropping in 2003.³⁴ From 2003 to 2005, vacancy rates increased slightly for *technologists/scientists* at all levels (i.e., staff, supervisory, and managerial), and increased for *technicians* at the supervisory level (including phlebotomists).

ASCP identified several trends in vacancy rates by laboratory setting:

- Reference laboratories had higher-than-average vacancy rates for certified technologists/scientists and technicians.
- Hospital-based laboratories reported slightly higher-than-average vacancy rates for phlebotomy staff and supervisors.
- Vacancy rates for certified HTLs and HTs were higher for laboratories housed in facilities with 500 beds or more. These laboratories also reported higher-than-average vacancy rates for certified technologists/scientists staff and supervisors.
- Laboratories located in the northeastern U.S. reported high vacancy rates for certified HTLs.
- Vacancies for certified technologists/scientists staff were higher than average in the far western and northeastern U.S., while vacancies for certified phlebotomy staff were highest in the far western U.S.^{c,34}

^c California recently began requiring certification of phlebotomists and imposing more stringent regulations regarding phlebotomy certification.³⁸ The higher-than-average vacancy rate among phlebotomy staff in the far western U.S. may be attributable to California's phlebotomy certification requirement.

Table 3.1: Vacancy Rates for Various Clinical Laboratory Personnel Positions in the U.S. Selected Years 2000-2005

Position	2000	2002	2003	2005
Medical Technologist/Clinical Laboratory Scientist				
Staff	11%	7%	4%	6%
Supervisory	13%	6%	3%	4%
Manager	13%	4%	2%	4%
Medical Laboratory Technician/Clinical Laboratory Technician				
Staff	14%	9%	6%	6%
Supervisory	n/a	7%	2%	3%
Phlebotomist				
Staff	18%	9%	7%	7%
Supervisory	n/a	8%	3%	5%
Histologist				
Histotechnician	16%	9%	6%	4%
Histotechnologist	22%	11%	4%	7%
Supervisory	20%	6%	5%	4%
Cytologist				
Staff	21%	8%	4%	3%
Supervisory	10%	6%	2%	2%

Source: Steward CA, Thompson NN. ASCP 2005 wage and vacancy survey of medical laboratories. *Laboratory Medicine* 2006;37(8):465-469.

Note: Vacancy rates varied by geographic region.

WAGES

Pathologists

Pathologists earn salaries comparable to other physicians. Starting salaries for most pathologists exceed \$125,000 per year and vary by geographic region and place of employment.³ The ASCP's 2006 job market survey asked pathology residents and fellows about their job offers.³⁶ Of those respondents who had been offered a job, including both residents and fellows in their final year of training, 12% were offered less than \$100,000 per year, 39% were offered a salary that ranged from \$100,000 to \$150,000, 44% were offered a salary between \$150,000 and \$200,000, and 5% were offered a salary greater than \$250,000. After their first and second year of training, another study of allied physicians found that pathologists earned a base salary of \$169,000; those with more than three years of practice earned \$321,000.^{d,39} In 2007, the Medical Laboratory Observer annual survey of 1,873 laboratory personnel found that the median annual salary of pathologists was \$190,000.⁴⁰ Table 3.2 provides summary data^e compiled by the Modern Healthcare Physician

^d This survey did not report whether figures represented median or average incomes.

^e The following surveys were included in the data: American Medical Group Association: data from more than 32,000 member medical group physicians in 123 specialties. Hay Group: surveyed 98 organizations. Hospital and Healthcare Compensation Service: 17,650 physicians in 44 specialties. Medical Group Management Association: 40,295 physicians in more than 105 specialties. Sullivan, Cotter and Associates: more than 175 organizations. Warren Surveys: more than 7,000 physicians in 32 specialties. Merritt, Hawkins and Associates: 2,687 physicians.

Compensation Review of pathologist salary ranges from seven different survey instruments as reported in 2005.

Table 3.2: Comparison of Pathologist Salary Ranges to Other Physician Groups, 2005

Physician Specialty	Salary Range
Pathology	\$193,477 - 350,286
Anesthesiology	\$274,886 - 338,722
Cardiology	\$287,907 - 387,800
Internal Medicine	\$163,250 - 180,800
Obstetrics/Gynecology	\$222,838 - 275,800
Oncology	\$241,628 - 320,200
Pediatrics	\$144,000 - 184,900
Radiology	\$209,365 - 411,131

Source: 2005 Modern Healthcare Physician Compensation Review. Irving, TX: Merritt, Hawkins & Associates, 2005.

Doctoral-Level Laboratory Scientists

Although salary information specifically for doctoral-level laboratory scientists is unavailable, surveys of laboratory directors and laboratory professionals with postgraduate degrees have been conducted. A 2004 survey of 2,128 laboratory professionals conducted by Medical Laboratory Observer found the median salary for laboratory directors was \$86,238, approximately 3% greater than the median salary reported in the 2003 survey.^{41, 42} Median salary for laboratory professionals with a postgraduate degree was \$76,454.

In addition, several organizations track salary information for professionals who have achieved doctoral-level chemistry and toxicology degrees. A 2006 salary survey conducted by the American Chemical Society, completed by 8,580 respondents, found that the median base salary for professionals with doctoral-level chemistry degrees was \$95,000.⁴³ Average annual salaries increased by 3.4% between 1996 and 2006, adjusting for inflation. A 2004 survey of individuals with doctoral-level degrees in toxicology conducted by the American College of Toxicology and the Society of Toxicology found that salary varied by years of experience following terminal degree and by sex.⁴⁴ Mean annual salary for individuals employed in contract laboratories with three to five years experience was \$81,000 for men and \$90,000 for women; mean annual salary for individuals employed by the federal government with three to five years experience was \$78,000 for men and \$75,000 for women.

Technologists/Scientists and Technicians

Significant differences in salary for technologists/scientists are based on education, geographic location, job function, and work experience.⁴⁰ Nationally, annual salaries in 2005 ranged from \$24,419 for staff phlebotomists to \$66,539 for technologist managers.³⁴ Laboratory employees with a postgraduate college degree made about \$22,000 more than employees with a high school diploma. Table 3.3 provides specific wage information delineated according to position.

ASCP found that the median average hourly salaries for personnel working in hospital-based and reference laboratories were more likely to be higher than personnel working in POLs.³⁴ Salaries

also were higher in larger laboratories whose test volume exceeded one million tests per year. Other data indicate that most laboratory technologists/scientists working with management and technical consulting services earned higher wages. Yet, laboratory managers and administrators and information systems managers earned more money on average than medical technologists, section managers and section manager supervisors.⁴⁰

Geographic assessment of wages indicate that California, Alaska, and Nevada were the top-paying states for technologists/scientists, whereas Rhode Island, Alaska, and Hawaii were the top-paying for laboratory technicians.^{17, 18} Conversely, professionals working in the mountain and southeast areas of the U.S. were paid less on average than those in other regions.

Table 3.3: Median Average Wages for all Clinical Laboratory Positions and Levels in the U.S., 2005

Position	Median Average Annual Salary*
Technologist/Scientist	
Staff	\$44,762
Supervisory	\$53,997
Manager	\$66,539
Technician	
Staff	\$35,838
Supervisory	\$41,642
Phlebotomist	
Staff	\$24,419
Supervisory	\$34,923
Histologist	
Histotechnologist	\$44,990
Histotechnician	\$38,418
Histotechnician- Supervisory	\$54,018
Cytologist	
Staff	\$54,434
Supervisory	\$63,523

*Median average annual salary calculated from median average hourly wage using assumption that employees are working 2,088 hours per year, or 40 hours per week for 52 weeks.

Source: Adapted from Steward CA, Thompson NN. ASCP 2005 wage and vacancy survey of medical laboratories. *Laboratory Medicine* 2006;37(8):465-469.

EDUCATION, TRAINING, AND RECRUITMENT

Medical Schools

The educational requirements for pathologists, whether for an Doctor of Medicine (MD) degree or Doctor of Osteopathy (DO) degree, match those of all medical doctors, which include pre-medical school requirements, four years of medical school, and three-to-six years of post-graduate training.^{3,45} For purposes of comparison, allopathic medicine (traditional medicine) is characterized as using remedies to counter the effects produced by the disease and emphasizes diagnosis and treatment of specific diseases within the body.^{46,47} Traditional allopathic medical school curricula consist of two years of basic science education and two years of clinical rotations. Osteopathic medicine is characterized by its emphasis on the connection between structure and function and the body's inherent ability to heal itself.⁴⁸ Similar to MDs, doctors of osteopathic medicine can choose any medical specialty, prescribe drugs, perform surgery, and practice medicine anywhere in the U.S.⁴⁹ Schools for osteopathic medicine also require two years of basic science education followed by two years of clinical clerkships and three-to-six years of post-graduate training.⁵⁰

Current data indicate that:

- There are 148 medical schools in the U.S., of which 125 teach allopathic medicine and 23 teach osteopathic medicine.^{51, 52} In 2006, an estimated 69,167 students were enrolled in allopathic medical schools, a 5% increase since 2002.⁵³ Male-female ratios were relatively even (49% female).
- Enrollment in osteopathic schools of medicine, which totaled 13,406, grew at a substantially higher rate of 17% during this same period.^{54,55} Approximately 50% of all osteopathic medical school students were female.

The need for more physicians in the U.S. and predictions of physician shortages are contributing to a push for increased enrollment in medical schools. The Council on Graduate Medical Education, an advisory group to the Health Resources and Services Administration, has recommended that allopathic and osteopathic medical schools increase their enrollment by 15% from their 2002 levels over the next 10 years, both by expanding the size of first-year classes and by building new medical schools.⁵⁶ Emphasis on recruitment and enrollment are proving successful.

- In 2007, a total of 42,315 people applied to allopathic medical schools, an increase of 8% since 2006.⁵⁷ Earlier data (2005) found a similar trend with osteopathic medical schools, which received 8,258 applications, a 14% increase over the previous year.⁵⁸
- Actual enrollments in medical school are projected to increase. First-year enrollment in allopathic medical schools is expected to increase by 17% to nearly 19,300 students by 2012.⁵⁹ Osteopathic medical school enrollment may double between 2002 and 2015.⁶⁰

Residency and Fellowship Programs

Following medical school, allopathic and osteopathic graduates can apply to pathology residency programs through the National Residency Match Program (NRMP), which is a private, not-for-profit corporation that provides a uniform date of appointment to all entering

medical residents.⁶¹ The length of time required to complete residency and post-graduate training in pathology ranges from three to six years, depending on field of pathology in which a physician is specializing.⁴⁵ Residency programs that combine clinical and anatomic pathology require four years of training, while those that focus on either clinical or anatomic pathology require three years. Training in a specific pathology subspecialty requires an additional year, with the exception of neuropathology which requires an additional two years. Residency programs for pathology have not been developed by osteopathic-related organizations. As a result, osteopathic graduates must enter NRMP allopathic residency programs in order to practice pathology. However, the Osteopathic Postdoctoral Training Institute-West^f is developing pathology residencies in California and Oregon.^{62, 63}

Residency Programs

As of 2007, there were 150 NRMP-accredited anatomic and clinical pathology residency programs.⁶ In 2006, there were an estimated 2,603 active pathology residents and fellows.³⁶ There are notable differences in trends between the 2001-2005 and 2005-2007 periods, as follows.

- The total number of pathology residency positions offered through the NRMP increased from 383 to 526 positions from 2001 to 2005, but decreased by 13 positions between 2005 and 2007.⁶⁴
- The number of allopathic medical school seniors entering pathology residency programs increased by an average of 19% annually from 2002 to 2005, but decreased by an average of 5% from 2005 to 2007.⁶⁵ Still, only about 2% of all medical students enter pathology residencies.⁶⁴
- Allopathic seniors filled 50% of pathology residency positions in 2002, and 55% in 2007.⁶⁴ Graduates of international and osteopathic medical schools and prior graduates of allopathic medical schools filled approximately 34% of pathology residency positions in 2002 and 33% in 2007.^{64, 65}
- Approximately 9% of pathology residency positions remained vacant in 2007, compared to 16% in 2002.
- Fewer than 1% of osteopathic graduates have chosen a career in pathology during the past 10 years.⁵⁴

Fellowship Programs

Following completion of a pathology residency, many physicians pursue specialty training through fellowship programs. According to the ASCP's 2006 job market survey, which was completed by 742 residents in their final year of training, 702 applied for fellowships.³⁶ More than half of respondents attributed their pursuit of fellowship training to their long-term career interests; 29% indicated that the completion of a fellowship was necessary to secure eventual employment in their desired position. Subspecialty training programs and enrollment for residents and fellows for pathology programs leading to subspecialty certification are provided in Table 3.4.

^f Osteopathic Postdoctoral Training Institute is an educational consortium with 8 member institutions that supports osteopathic graduate medical education programs in the western U.S.

Table 3.4: Number of Accredited Pathology Specialty Programs and Total Number of Active Residents/Fellows in Program in the U.S., 2006^g

Pathology Specialty	Number of Accredited Programs	Total Number of Active Residents/Fellows in Program
Blood Banking/Transfusion Medicine	46	36
Chemical Pathology	3 ^h	2
Cytopathology	85	109
Dermatopathology	47	51
Forensic Pathology	38	28
Hematology	77	88
Medical Microbiology	12	9
Molecular Genetic Pathology	18	12
Neuropathology	35	38
Pediatric Pathology	25	18

Source: FREIDA online specialty training statistics information. Chicago, IL: American Medical Association, 2005. Accessed February 28, 2007. <http://www.ama-assn.org/vapp/freida/spcstsc/0,1238,300,00.html>.

Doctoral-Level Laboratory Science Programs

Professionals can enter the laboratory workforce as graduates of doctoral programs in laboratory-related fields such as clinical chemistry, toxicology, and microbiology. Requirements for entry into doctoral programs vary according to the institution, but most U.S. science graduate programs require applicants to have completed a bachelor's and/or master's degree and required entrance examinations.^{67, 68}

Doctoral study typically involves three stages of academic work.⁶⁹ The first stage consists of preliminary course, seminar, and laboratory studies. The second stage includes a set of advanced seminars and consortia during which students select a dissertation subject and design their research. Independent research as well as the writing, presentation, and defense of the thesis encompass the final stage of doctoral education. A doctorate of philosophy or doctorate of scienceⁱ in a laboratory-related subject area is required for board certification.^{70, 71}

Most laboratory doctoral scientists also complete postdoctoral fellowships that last one or two years and prepare them to serve as a director and/or laboratory consultant in a variety of laboratory settings, including microbiology, immunology, and public health laboratories.⁷² Postdoctoral fellowship programs are accredited by a variety of professional societies. For example, there are currently 12 postdoctoral training programs located in medical centers across the U.S. approved by the American College of Microbiology's Committee on Postgraduate Educational Programs.⁷³ The Commission on Accreditation in Clinical Chemistry currently accredits postdoctoral fellowship training programs at 18 institutions across the U.S. and Canada.⁷⁴

^g There is no subspecialty certification program for surgical pathology; therefore, it was not included in this table.

^h The Accreditation Council for Graduate Medical Education only recently began accrediting chemical pathology programs and, thus, the number of programs is currently low but expected to increase in coming years.⁶⁶

ⁱ In some cases, individuals who have earned a doctoral-level degree in osteopathic medicine, veterinary medicine, public health, or dental surgery can be accepted for board-level certification as a doctoral-level laboratory scientist if they have met the requirements for postdoctoral training and laboratory-related experience.⁷⁰

A total of 15,560 doctoral degrees were awarded in biology, biomedicine, health and clinical science, physical science, and science technologies during the 2004-2005 academic year, an increase of approximately 16% relative to 2003-2004.⁷⁵ About 61% were awarded by public universities. Degrees awarded in these areas represent approximately 28% of all doctoral degrees. This percentage is representative of the overall increase in doctoral degrees awarded over the past 25 years, as life sciences doctorates have increased 57% and physical sciences doctorates have increased 30%.^{30,31} However, these professionals are not necessarily eligible to perform the duties of a doctoral-level laboratory scientist.

ASCLS and other organizations are developing educational programs that lead directly to a doctorate in clinical laboratory science (DCLS).⁷⁶ The DCLS would provide an alternative to traditional master's and research-based doctoral degrees. The National Accrediting Agency for Clinical Laboratory Sciences (NAACLS) approved standards for accreditation of DCLS programs in September 2006 and began reviewing applications for programs interested in offering the DCLS degree in April 2007.⁷⁷

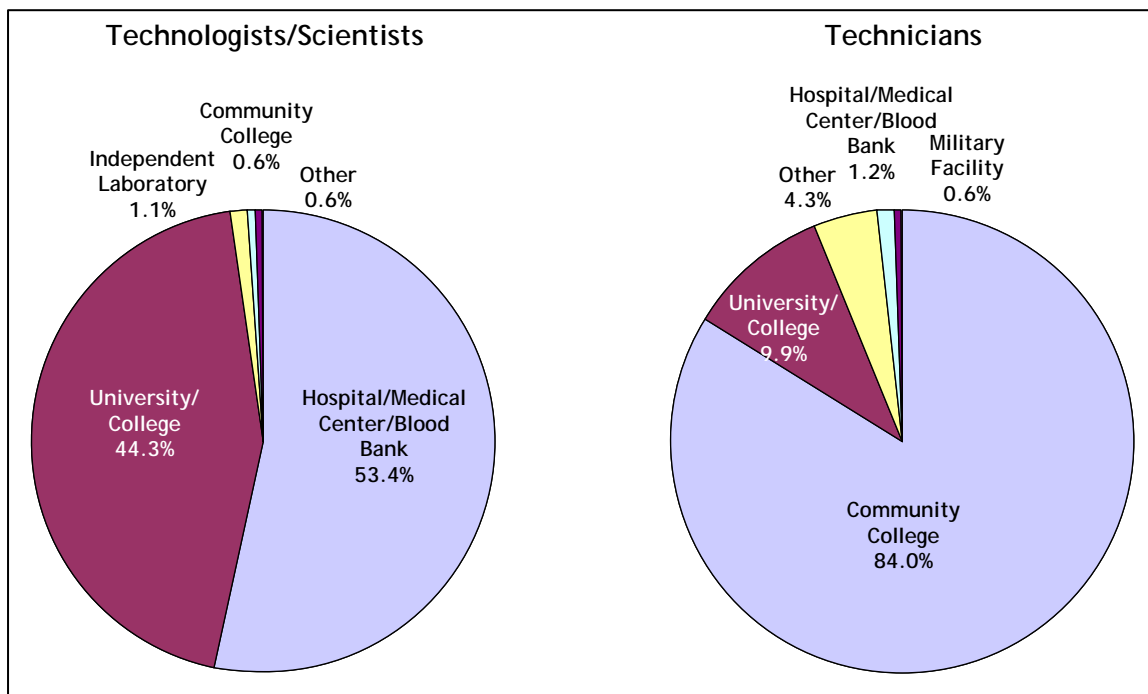
Technologist/Scientist and Technician Education Programs

Educational requirements for technologists/scientists are more stringent than those for technicians. Becoming a technologist requires a bachelor's degree in medical technology, clinical laboratory science, or one of the life sciences.^{1,15} Technicians, on the other hand, typically have an associate's degree from a junior or community college or training from a hospital, a technical or vocational school, or from the U.S. Armed Forces.¹⁵ It also is possible to become a technician without obtaining an associate's degree by completing required coursework in biology and chemistry at an accredited college or university.¹³ Along with formal training, both technologists/scientists and technicians must complete additional clinical education in a medical technology or clinical laboratory science program accredited by NAACLS.^{j16} Depending on the state in which they practice and the setting in which they work, further training beyond these requirements may be necessary.

As depicted in Figure 3.3, the majority of these educational opportunities are provided in hospital-based programs, universities, and community colleges.⁷⁸ There are clear differences in educational sites between technologist/scientist programs and technicians.

^j Depending on the route followed, not all certified technologists/scientists and technicians complete NAACLS-accredited programs. For example, some technicians have an associate's degree or 60 semester hours of academic credit, have completed required coursework, and have completed a 50-week U.S. military medical laboratory training course.

Figure 3.3: Educational Program Settings for Technologists/Scientists and Technicians, 2006



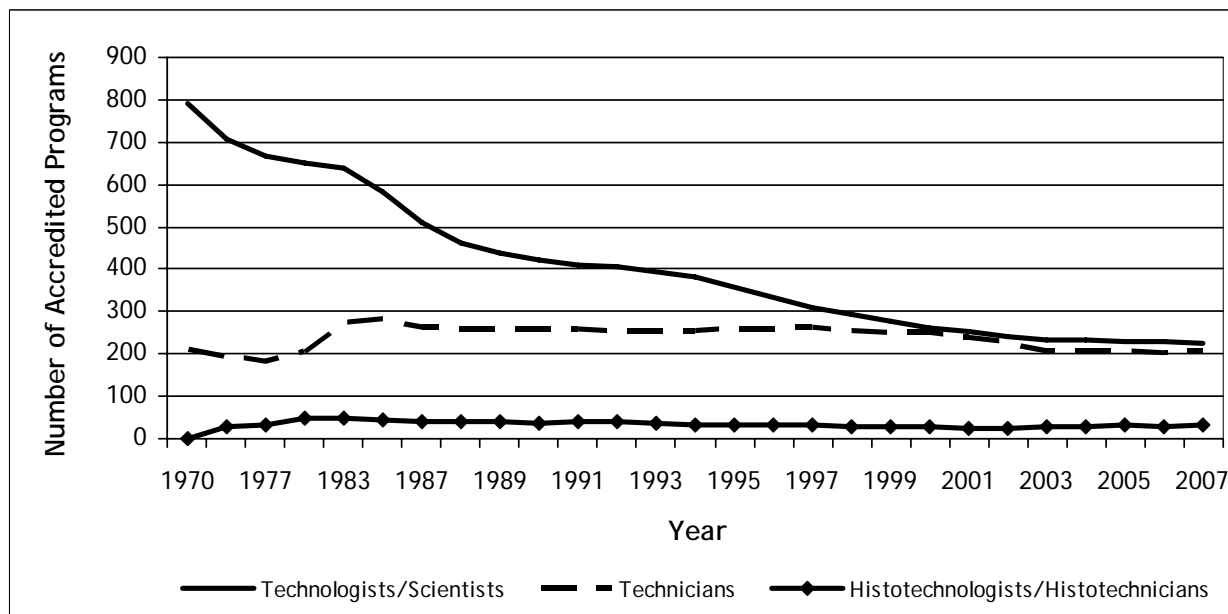
Source: Bugbee AC. ASCP Board of Registry's 2006 annual survey of medical laboratory science programs. *Lab Medicine*, 2007;38(8):463-471

Programs

All technologist/scientist and technician education programs must be accredited by the NAACLS or the Commission on Accreditation of Allied Health Education Programs.¹ NAACLS accredits more than 469 programs for technologists/scientists and technicians, HTLs, HTs, pathologists' assistants, diagnostic molecular scientists, cytogenetic technologists, and phlebotomists.^{15,79} The Commission on Accreditation of Allied Health Education Programs accredits 47 programs in cytotechnology and 15 programs for blood banking specialists.^{80,81} Figure 3.4 portrays trends in the numbers of NAACLS-accredited education programs for specific laboratory professional groups between 1970 and 2007. Among these trends:

- The number of education programs for technologists/scientists and technicians have declined since 1975, and enrollment in these programs has declined over 50% since 1980. (See discussion on student population.)^{1,82}
- The most dramatic decline has been in technologists/scientists programs, approximately 71% of which closed between 1970 and 2007.⁸³ Four programs closed between 2006 and 2007 alone.
- From 1985 to 2007, the number of technician education programs declined by approximately 27.0%. However, four new programs were created during 2006-2007.
- Declines in the number of education programs fall into specific disciplines. The number of HTL and HT programs diminished from 49 in 1983 to 30 in 2006, a decline of 38.8%, while the number of phlebotomy training programs increased six-fold, from 9 to 58 from 1987 to 2003.

Figure 3.4: Trend in Number of NAACLS-Accredited Education Programs in Clinical Laboratory Sciences, 1970-2007



Source: NAACLS table of program and graduate numbers. Tice D, ed. Chicago, IL: National Accrediting Agency for the Clinical Laboratory Sciences, 2007.

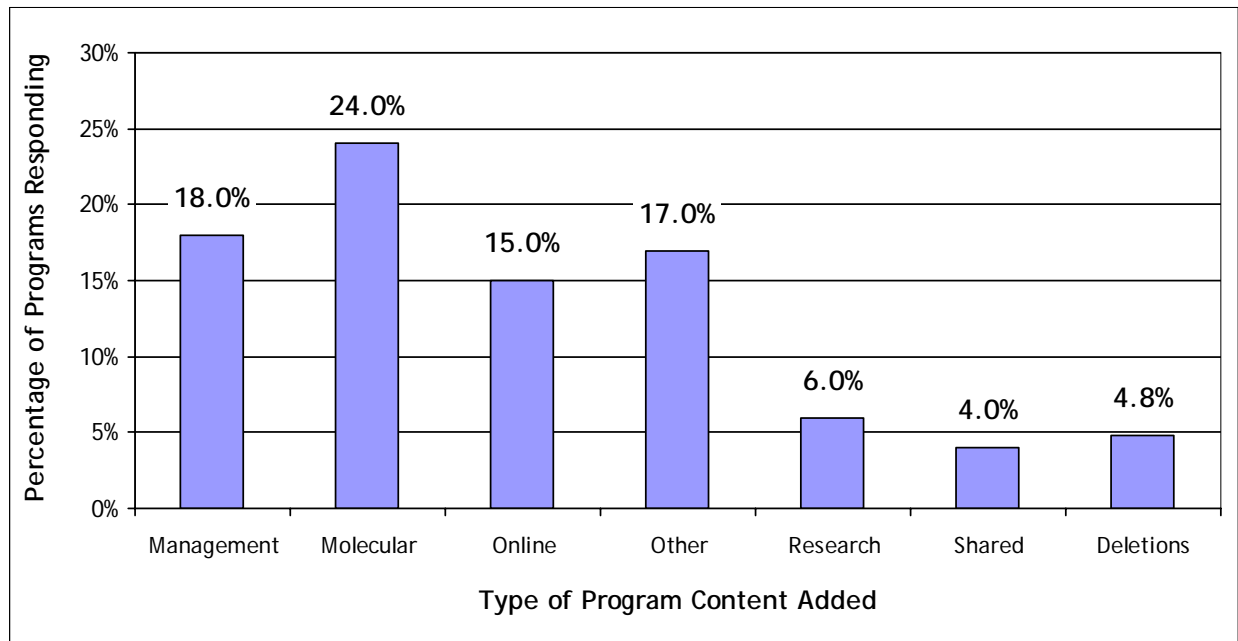
A variety of factors have affected the laboratory medicine educational programs. The Medicare Prospective Payment System changed the hospital payment structure such that clinical laboratories (including outreach testing), once a source of revenue, became cost centers.⁸² Increases in treatment via the outpatient setting further decreased hospital revenue by diminishing the number of inpatients requiring laboratory tests. Other factors often cited as reasons for the decline in laboratorian education programs include their operating expenses, the number of different instructors and faculty members required, and the lack of outside funding. The decreasing number of students entering laboratorian education programs is attributed to additional factors. Historically, women have dominated the technologist/scientist and technician workforce; however, as wider employment opportunities have arisen, they have been entering other positions in science and medicine. Salary and career advancement opportunities associated with laboratory medicine often are less desirable than those in other health-related industries. Work schedules for laboratorians, which can require long hours and overnight shifts, may be less attractive than for some other health professions and other competing employment opportunities.^{1,84}

Curriculum

Due to the changing nature of laboratory medicine (e.g., increases in genetic testing, increased use of technology systems and automation), more than half of all medical laboratory science program directors have reported changes to the educational curriculum in 2002, the last year that this data was reported by ASCP. Among programs reporting curricular changes, approximately 24% adjusted molecular science content, 18% changed management skills content, and 15% altered online content during the 2002-2003 academic year (Figure 3.5).⁸⁵ Fewer than 5% of programs reported deleting any curricular content. The long-term benefit of these changes is unclear at this time.

Proposals for widespread, systemic changes include raising awareness of clinical laboratory professional's role in health care, lowering the operational costs of training programs (e.g., incorporating distance learning, founding education programs at independent laboratories), and educating laboratory professionals in new technology-related areas such as POCT and informatics.^{1, 82}

Figure 3.5: Percentage of Technologist/Scientist and Technician Programs Reporting New Content to Curricula, 2002



Source: Ward-Cook K, Chapman S, Lindler V. Executive summary: 2002 annual survey of accredited/approved medical laboratory science programs. Chicago, IL: American Society for Clinical Pathology, 2002. <http://www.ascp.org/Certification/ForProgramDirectors/research/documents/Svy02.pdf>

Student Population

Enrollment

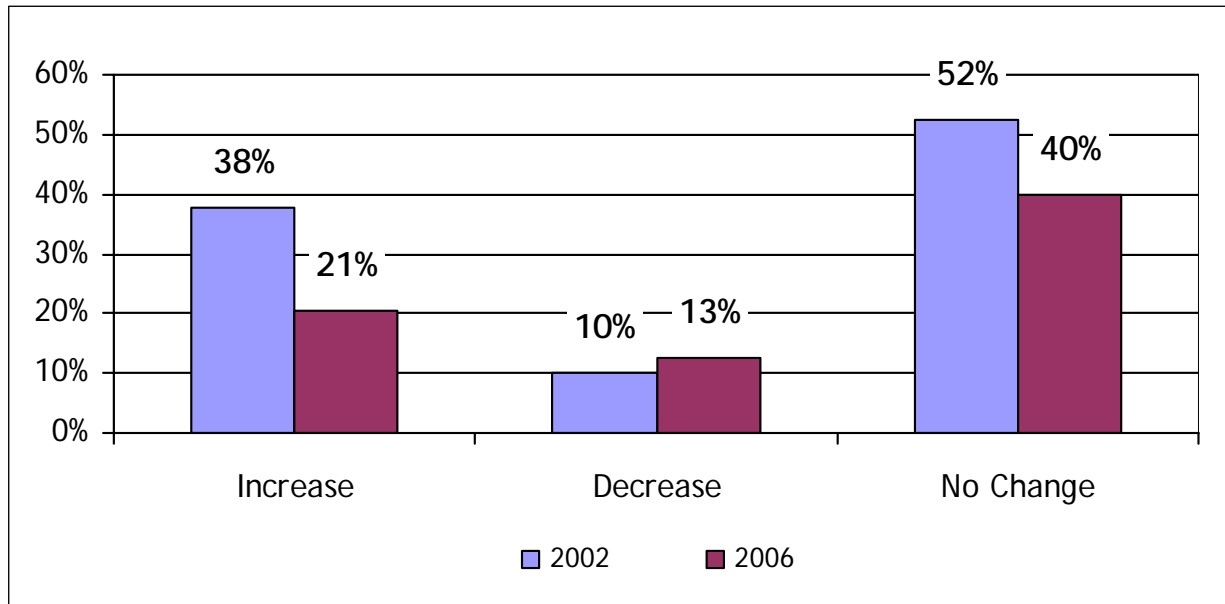
Data on the number of students entering technologist/scientist, technician, and HT/HTL programs are available only through 2002.^k In this year, a total of 4,782 students entered NAACLS-accredited programs for technologist/scientist, technician, and HT/HTL.^{1, 83} In that year, 3,974 graduated.

Of students entering laboratory medicine education programs, 40% entered technologist/scientist programs, 54% entered technician programs, and over 5% entered HT/HTL programs. Recruitment efforts targeting minorities and males have resulted in recent increases in enrollees for blood banking and histotechnology. Given the importance of active recruitment, about half of programs have staff and one-third have special budgets dedicated to recruiting new students.

^k Although NAACLS collects enrollment data, there are discrepancies in defining point of enrollment that affect counts (i.e., according to when the enrollee begins their education, enters the professional sequence, or enters the clinical sequence). For this reason, this enrollment data are used only internally by NAACLS.⁸³

A 2006 survey that examined medical laboratory science program directors' perceptions of the quality of applicants found that about 40% perceived no change in quality, 21% perceived an increase in quality, and 13% perceived a decrease in quality. The remaining 27% gave more than one answer to this question. Figure 3.6 provides a comparison of program directors' perceptions in 2002 and 2006.^{78,85}

Figure 3.6: Change in Quality of Applicants as Perceived by Laboratory Science Program Directors, 2002 and 2006



Note: Percentages for 2006 do not add to 100 because some respondents gave more than one answer.

Sources: Ward-Cook K, Chapman S, Lindler V. Executive summary: 2002 annual survey of accredited/approved medical laboratory science programs. Chicago, IL: American Society for Clinical Pathology, 2002. <http://www.ascp.org/Certification/ForProgramDirectors/research/documents/Svy02.pdf>

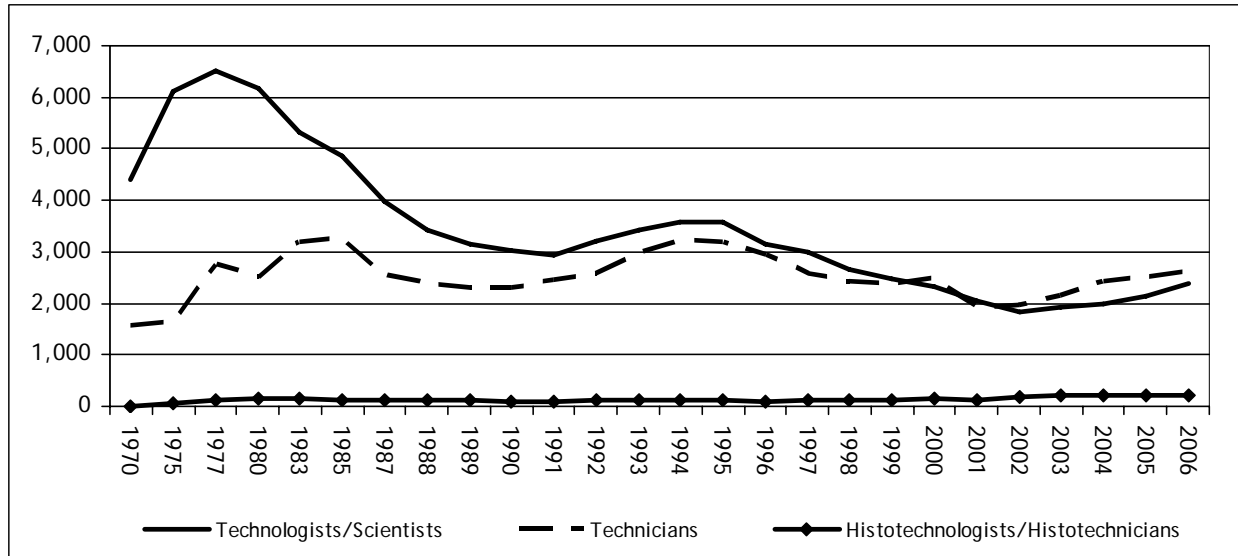
Bugbee AC. ASCP Board of Registry's 2006 annual survey of medical laboratory science programs. *Lab Medicine* 2007;38(8):463-471.

Graduates

There have been two periods of steep decline in the number of graduates from laboratory education programs. The first was a decrease of 42% that occurred from 1977 to 1990; the second was a decrease of 45% that occurred from 1994 to 2002.⁸³ Since 2002, the number of graduates has increased steadily by about 7% per year. Figure 3.7 shows the student populations graduating from NAACLS-accredited technologist/scientist, technician, and HT/HTL programs for the years 1970 through 2006.

Concerted efforts to promote laboratory programs have succeeded in increasing some graduate rates. Since 2002, the numbers of technologist/scientist and technician graduates have increased 30% and 33%, respectively.⁸³ The number of HT/HTL graduates increased by 17% from 2001 to 2003, then declined by 11% from 2004 to 2006. As noted above, these changes have accompanied the decrease in number of programs.

Figure 3.7: Graduates of NAACLS-approved Technologists/Scientists, Technicians, and Histotechnologists/Histotechnicians Programs by Program, 1970-2006



Source: NAACLS table of program and graduate numbers. Tice D, ed. Chicago, IL: National Accrediting Agency for the Clinical Laboratory Sciences, 2007.

LICENSING AND CERTIFICATION

State licensure and certification requirements for laboratory directors are embodied in the CLIA regulations and are based on the type of testing performed in the laboratory. Laboratories performing only waived tests do not have requirements for laboratory directors or other personnel.⁸⁶

Licensure

Licensure, sometimes referred to as “right of practice,” is the most restrictive form of professional and occupational regulation.¹ CLIA requires state licensure for individuals serving as directors of PPM laboratories and clinical consultants and for individuals with MD or DO degrees serving as directors of non-waived laboratories.^{9, 87, 88} Under CLIA, laboratory personnel performing PPM testing must also be licensed to practice in their state.⁸⁹ CLIA does not require licensure of doctoral-level laboratory scientists.

Pathologists

As with all physicians, pathologists must receive a medical license to practice. Licensure for physicians is granted by state boards of medicine and is required to guarantee to the public that a physician has successfully completed medical education and passed an examination or other form of certification demonstrating competency and appropriate qualifications to practice medicine.⁹⁰ All states, the District of Columbia, and the U.S. territories, a total of 54 jurisdictions, require

physicians to be licensed before they can legally practice medicine.^{91,1} A license is necessary for *each* state in which a physician wishes to practice. According to the Federation of State Medical Boards and the Bureau of Labor Statistics, physicians must provide proof of graduation from an accredited medical school, complete at least one year of residency training, and pass a licensing examination.^{90,91} Physicians who were educated outside of the U.S. or Canada are required to complete a residency in the U.S. prior to obtaining a license to practice medicine in the U.S., even if they are licensed to practice in another country.⁹⁰

There are no licensure requirements for doctoral-level laboratory scientists.

Technologists/Scientists and Technicians

In recent years, several state-based initiatives have been undertaken to institute licensure requirements for technologists/scientists and technicians. Table 3.5 summarizes current status of licensure activities.

Table 3.5: Status of Licensure Requirements for Technologists/Scientists and Technicians by State, 2007

Licensure of Laboratory Personnel Required	Licensure Legislation Introduced/Will Be Introduced in Next Legislative Session	Considering a Licensure Initiative
California	Illinois	Indiana
Florida	Massachusetts	Iowa
Georgia	Michigan	Nebraska
Hawaii	Minnesota	Virginia
Louisiana	Missouri	Wisconsin
Montana	Ohio	
New York	Texas	
Nevada		
North Dakota		
Rhode Island		
Tennessee		
West Virginia		
Puerto Rico		

Source: Garrett P. American Society for Clinical Laboratory Science. Personal communication. December 10, 2007.

In licensure states, laboratorians can practice only in the areas for which they are licensed. Employers can hire only licensed individuals to complete tasks within the defined scope of the licensure. However, the provisions governing licensure can vary by state. Most states require licensed personnel to pay an annual or bi-annual licensing fee, participate in continuing education, and meet minimum educational and professional competency requirements.⁹³ Some states require fingerprinting, documentation of certification from an accredited certifying agency, and documentation of a defined number of hours of continuing education.

¹ State medical boards can prepare their own licensing examinations or they can administer one prepared by and purchased from a specialized agency, such as the U.S. Medical Licensing Examination or the Comprehensive Osteopathic Medical Licensing Examination.⁹²

Certification

Under CLIA, board certification is required for doctoral-level laboratory scientists, who are not previously grandfathered, to serve as laboratory directors or clinical consultants for non-waived testing laboratories.^{9, 87} Some routes by which a pathologist can serve as a laboratory director also require board certification.^{9, 87} Certification is a voluntary process for other clinical laboratory personnel (i.e., pathologists, technologists/scientists, and technicians) by which nongovernmental agencies grant recognition to professionals whose levels of competence meet specific standards.^{9, 15, 87, 94, 95}

Pathologists

Physicians wishing to practice a medical specialty in the U.S. can seek certification from 24 nationally recognized medical specialty boards.⁹⁶ Certification of physicians practicing in a specialty is recognized by physicians, health care institutions, insurers, and patients as proof of a physician's knowledge and skills. Although physician certification is not required by law, some health care plans provide additional benefits and recognition to physicians who are board certified and who maintain their certification.⁹⁷

The American Board of Pathology (ABP), under the American Board of Medical Specialties, provides primary certification in clinical pathology, anatomic pathology, or both.^m ABP also offers certification in 10 pathology subspecialties.⁹⁹ Examinations comprise written and practical components, both of which candidates must pass in the same sitting.⁹⁹ In order to apply for ABP certification, applicants must have graduated from a U.S. or Canadian medical school accredited by the Liaison Committee on Medical Education or from an osteopathic medical school accredited by the Bureau of Professional Education of the American Osteopathic Association (AOA). Applicants for primary and subspecialty certification also must provide proof of valid licensure to practice medicine in a state or jurisdiction of the U.S. or Canada.

The American Osteopathic Board of Pathology (AOBP), part of the AOA, is responsible for evaluation and recommendation of osteopathic physician candidates for certification in anatomic pathology, laboratory medicine, and forensic pathology.¹⁰⁰ In order to receive AOBP certification, candidates must be a graduate of an AOA-accredited college of osteopathic medicine, licensed in the state or territory of practice, a member of the AOA or the Canadian Osteopathic Association for two years prior to the date of certification, complete one year of AOA-approved internship plus four years of additional training in clinical or anatomic pathology, and provide evidence of conformity to the AOA Code of Ethics.¹⁰¹

Effective January 1, 2006, all primary and subspecialty certificates issued by the ABP expire after 10 years.¹⁰² Pathologists must fulfill requirements in key areas to be recertified.ⁿ Pathologists who received ABP certification prior to this date can participate in the maintenance of certification

^m The ABP administers all certification examinations in computer-based format at the APB Examination Center in Tampa, FL.⁹⁸ Primary certification examinations are offered twice a year; pathology subspecialty certification examinations in pathology, medical microbiology, molecular genetic pathology, neuropathology, and pediatric pathology are given every two years.

ⁿ ABP recertification requirements include: proof of unrestricted license to practice medicine; participation in continuing medical education; completion of a recertification exam; and provision of peer attestations of interpersonal and communication skills, professionalism, ethics, and effectiveness in systems-based practice.

program on a voluntary basis. Similarly, on January 1, 1995, AOBP's recertification^o requirements for osteopathic pathologists became valid for 10 years. However, for those certified prior to 1995, recertification is voluntary.

Doctoral-Level Laboratory Scientists

CLIA requires board certification for all doctoral-level laboratory scientists who are serving as a laboratory director and clinical consultant. Four organizations are currently approved by DHHS to certify doctoral-level laboratory scientists:

- American Board of Bioanalysis
- American Board of Clinical Chemistry
- American Board of Medical Laboratory Immunology
- American Board of Medical Microbiology

Candidates must demonstrate appropriate education, postdoctoral training, and laboratory experience.^{70, 71, 103, 104} The length of training or experience required varies by board and by the educational route chosen by the candidate (e.g., completion of a postdoctoral fellowship), but most boards require a minimum of three years of postdoctoral experience prior to certification. In some cases, individuals who participate in postdoctoral fellowships are eligible to apply for early admission to the examination. For example, applicants who have completed at least one year of a postdoctoral clinical chemistry training program accredited by the Commission of Accreditation in Clinical Chemistry are eligible to take the ABCC certification examination prior to completing their fellowship.^{p,103}

Candidates who have met all certification requirements are eligible to take a written certification exam. Candidates who pass the examination are recognized as diplomates. All four boards require diplomates to participate in continuing education programs in order to maintain certification. Table 3.6 displays the number of diplomates certified by each board in 2007 and the total number of active diplomates certified by each board.

The ABCC reports that, over the past 15 years it, has certified an average of 11 diplomates in clinical chemistry, 2 diplomates in toxicology, and 2 diplomates in molecular diagnostics.³⁷ According to this and other organizations, the number of diplomates has been decreasing over the past several years. As in other areas of laboratory medicine, the decrease is attributed to increases in use of advanced technology systems in the laboratory and market consolidation. Anticipated retirement of a significant number of doctoral-level laboratory scientists over the next several years is expected to increase the demand for new diplomates.

^o For AOBP recertification, osteopathic pathologists must: hold certification for at least 8 years; present written evidence of continuous compliance with the initial requirements of the AOA for specialty certification; and submit documents that provide evidence of having attended, presented, or participated in at least 75 hours of education programs, seminars, lectures, or other academic sessions relating to pathology or a division of pathology during the preceding three-year period.

^p After obtaining certification, these applicants must complete their fellowship and meet all requirements before becoming a director of a high complexity laboratory or a clinical laboratory consultant.

Table 3.6: Number of Diplomates Certified in 2007 and Total Number of Active Diplomates by Doctoral-Level Laboratory Scientist Certification Boards

	Number of Diplomates Certified in 2007	Total Number of Active Diplomates
American Board of Bioanalysis	Not Available	Not Available
American Board of Clinical Chemistry	16	346
American Board of Medical Laboratory Immunology	3	72
American Board of Medical Microbiology	25	310

Sources: ABCC register of active diplomates. Washington, DC: American Board of Clinical Chemistry, 2007.

ASM ABMLI diplomates database. Washington, DC: American Board of Medical Laboratory Immunology, 2007.

ASM ABMM diplomates database. Washington, DC: American Board of Medical Microbiology, 2007.

Technologists/Scientists and Technicians

Voluntary certification is the professional standard for technologists/scientists and technicians. Some employers require that employees maintain their certification for the duration of their employment. Organizations offering certification for these laboratorians include the:

- Board of Registry of the American Society for Clinical Pathology
- National Credentialing Agency for Laboratory Personnel
- Board of Registry of the American Association of Bioanalysts
- American Medical Technologists
- National Registry of Clinical Chemistry
- National Registry of Microbiologists¹
- State certification programs, such as that in California¹⁰⁵

The ASCP and the NCA provide the majority⁹ of certifications for technologists/scientists and technicians.¹ In 2006, ASCP certified 2,050 new technologists/scientists and 1,479 new technicians. From April 2006 through March 2007, NCA certified 312 new technologists/scientists and 121 new technicians.^{106, 107}

Technologists/scientists can earn ASCP specialty certification in blood banking, chemistry, cytology, hematology, histology, microbiology, hemapheresis, laboratory safety, virology, and molecular pathology.¹³ In some instances, categorical certification in one of these areas can be obtained without first becoming a certified (general) medical technologist/clinical laboratory scientist. For technicians, ASCP certification is available in apheresis, phlebotomy and donor phlebotomy, and histology.

In 2004, the ASCP initiated a certification maintenance program that extends three years and initially applied only to newly certified individuals in the entry level categories.¹⁰⁸ However, the requirement was extended to all individuals in 2006. ASCP certification maintenance varies

⁹ As of December 2006, the ASCP had certified a total of 223,958 technologists/scientists and 70,674 technicians.¹⁰⁶

NCA does not track the total number of professionals certified.¹⁰⁷ In general, among first-time takers of certification examinations, ASCP certifies approximately 2,000 technologists/scientists and 1,300 technicians each year, while NCA certifies approximately 655 technologists/scientists and 200 technicians annually.¹

according to certification type but generally involves participation in formal or employer-based continuing education courses relating to various aspects of the laboratory. The NCA began requiring certification renewal in 1980 via continuing education or re-examination.¹⁰⁹ Recertification by either method extends NCA certification by three years.

CONCLUSIONS

Clinical laboratories conducting non-waived testing typically are staffed with a medical team comprising pathologists, doctoral-level laboratory scientists, technologists/scientists, and technicians. While some of the tasks they perform on a daily basis may overlap, the contributions and responsibilities of each differ in several ways.

- Pathologists (medical doctors) and doctoral-level laboratory scientists operate at the highest levels within clinical laboratories, often serving as laboratory directors responsible for staff oversight, testing processes, quality control procedures, quality of patient care, and other functions. In 2005, there were an estimated 19,339 pathologists in the U.S.; 80% work in community practice. Minorities are under-represented in the discipline of pathology with 10% identified as Asian, 3% Hispanic, and 1% African American. Slightly over half of pathology residents are female.
- Approximately 160,760 medical technologists/scientists and 144,710 technicians were employed in the U.S. in 2006. While this workforce also is female dominated (74%), it is more representative of the diverse ethnic make up of the population with 12% Asian, 11% African American, and 7% Hispanic. Geographically, 58% of technologists/scientists work in an urban setting, 24% in suburban, and 18% in rural.
- Overall, the number of technologist/scientist and technician education programs has declined by over 50% since 1970, with the most dramatic decline in technologist/scientist programs – 71% closed between 1970 and 2007. In contrast, the number of phlebotomy programs increased six-fold from 1987 to 2003. Factors contributing to the changes include decreases in hospital revenues resulting from changes to the Medicare payment system as well as the expense of operating clinical laboratory science programs.
- Current enrollment in specialized technologist/scientist and technician educational programs is lowest in blood banking and histotechnology. However, recent recruiting efforts programs appears to be effective, specifically those targeted at recruiting minorities and male students, raising awareness of laboratory careers among students, and dedicating program staff and budget specifically to recruitment.
- At present, 12 states and one territory require licensure of technologists/scientists and technicians, and 12 other states are involved in some phase of licensure activity. However, the specific requirements for licensure vary by state.

Gaps, Needs, and Challenges:

- There is significant concern regarding the growing shortage of technologists/scientists and technicians, which is expected to worsen over the next decade. The shortages are attributed to the aging of the workforce, competing career opportunities, and difficulty recruiting and retaining staff. Although vacancy rates at the staff level were highest in

2000 (11 to 22%), they remained steady from 2002 to 2005 at an annual rate of 4 to 7%. Vacancies vary according to staff position, laboratory type and size, and geographic location.

- Technological advancement of laboratory testing, emerging pharmacogenomic and proteomic testing, and greater laboratory automation could change the qualifications required of next generation laboratory professionals. The laboratory sector needs to clearly redefine staffing qualifications and workforce level requirements to meet these forthcoming advancements.

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CHAPTER IV

QUALITY AND THE TOTAL TESTING PROCESS

Improving quality has been a core goal of the laboratory medicine sector for decades, beginning with proficiency testing (PT) in the 1930s.^a Quality-related initiatives have been an important part of laboratory operations ever since.

A milestone in quality improvement occurred in 1986, when CDC hosted the first in a series of Institutes on Critical Issues in Health Laboratory Practice devoted to improving laboratory quality.¹ Representatives assembled from diverse sectors within the health laboratory community including laboratorians, providers, public health practitioners, industry representatives, regulators, and payers. Participants defined the roles and responsibilities to be assumed in the processes associated with laboratory testing. At this critical meeting, participants were introduced to the concept of the total testing process (TTP), a systems-based framework for examining all possible interactions and activities that can affect the quality of laboratory tests.¹ The aim of introducing the TTP was to design and implement interventions, restrictions, and limits that could reduce or eliminate errors that adversely affect testing and patient health outcomes.

Today, the TTP remains the conceptual framework for understanding the dynamics of laboratory medicine as well as quality measures to improve care. This chapter provides an overview of the TTP and examines the main types of error and other challenges to quality that occur in each phase.

DEFINITION OF THE TOTAL TESTING PROCESS

The initial definition of the TTP espoused at the 1986 CDC Institute still serves as the primary point of reference for addressing quality in laboratory medicine. Since its inception, the definition has been refined and expanded to encompass all components that complete the test cycle, from the point of the clinical question to the point of clinical action, known as the “brain-to-brain” model.² In this regard, the TTP is defined by the activities in three distinct phases that align with clinical workflow outside and inside the laboratory:

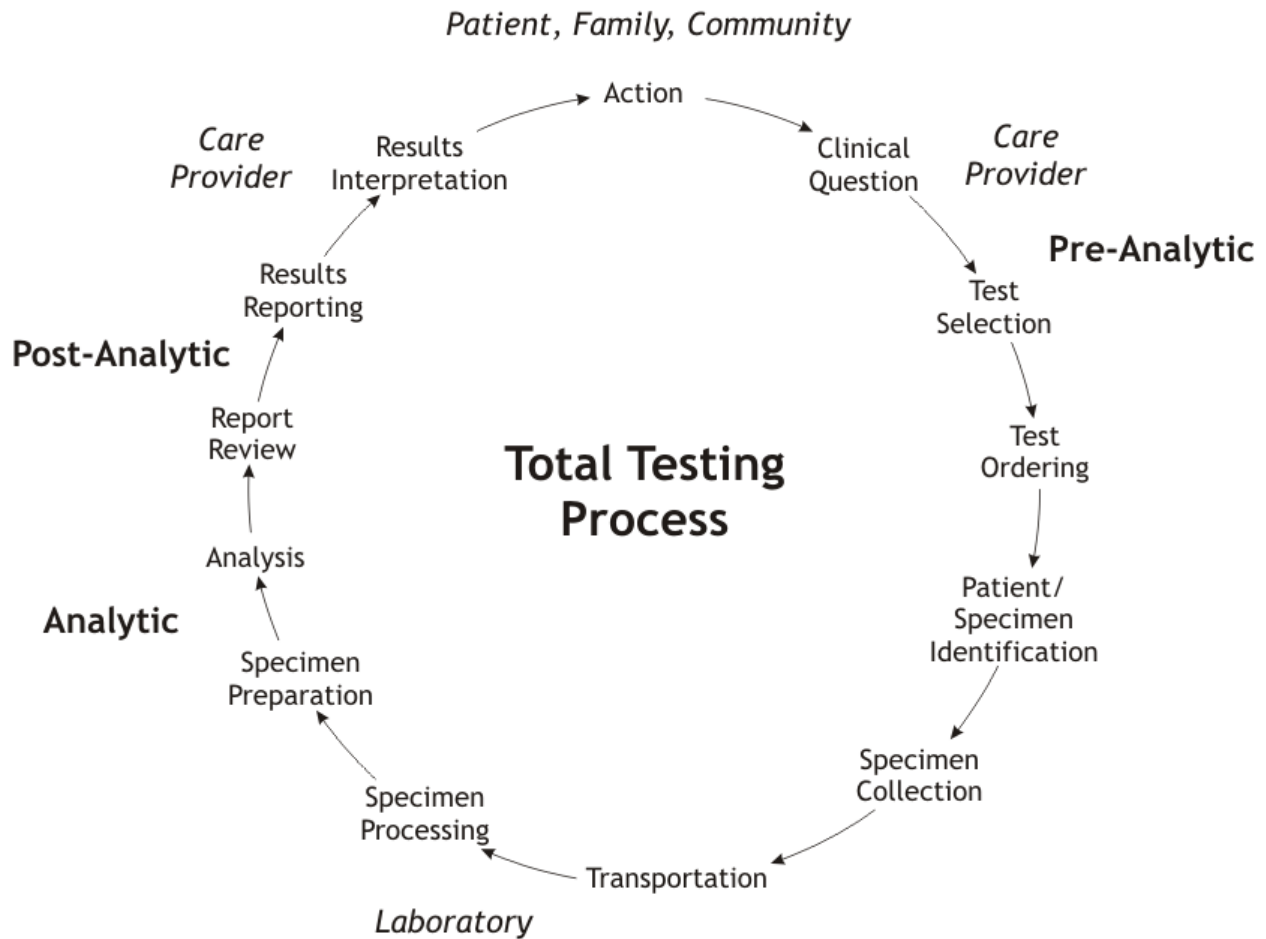
- (1) Preanalytic: clinician test selection, test ordering, patient preparation, specimen collection, patient and specimen identification, and specimen transport
- (2) Analytic: specimen processing and preparation, testing of the specimen, results review and verification, and quality control (QC) checks
- (3) Postanalytic: TAT, critical value reporting, report formatting, general results reporting, clinician interpretation and follow-up, laboratory interpretive consultation services, specimen storage and, if applicable, daily laboratory shutdown^{3, 4}

In most instances, preanalytic activities occur outside the laboratory. The specimen is collected by the clinician at the site of care (e.g., hospital, physician’s office, patient’s home). However, there are instances in which the specimen is collected at the laboratory. Some experts in laboratory medicine include specimen preparation in preanalytic activities. In the “brain-to-brain” model,

^a Further discussion on the history and development of quality-related initiatives in the laboratory sector is provided in the Quality Systems and Performance Measurement Chapter and Federal Regulatory Oversight Chapter of this report.

these activities are identified as analytic-related and, therefore, will be included in the discussion of the analytic phase for the purposes of this report. Similarly, postanalytic activities that involve laboratory communication with clinicians take place in both practice areas. Figure 4.1 presents a streamlined diagram of the key components of each phase of the TTP.

Figure 4.1: Phases of the Total Testing Process



Source: Adapted from Boone J. Presentation at the Institute on critical issues in health laboratory practice: managing for better health, September 23-26, 2007. Atlanta, GA: Centers for Disease Control and Prevention.

QUALITY AND ERRORS

Most quality initiatives in laboratory medicine have focused, historically, on the analytic phase of testing; however, root cause analyses and other medical error studies confirm that more errors occur in the preanalytic and postanalytic phases of testing. The distribution of these errors by phase varies among settings and institutions. An extensive review of reported errors in laboratory medicine published from 1992 to 2001 found great heterogeneity in study designs and reporting of errors. The distribution of errors was 32-75% in the preanalytic phase, 13-32% in the analytic phase, and 9-31% in the postanalytic (administration) phase.⁵ This review included studies of error rates associated with clinical chemistry, the whole laboratory, primary care, stat laboratory, and molecular genetic testing. One of these studies (whole laboratory) estimated that 8% of errors had the potential for serious harm.⁶ Error distribution in transfusion medicine is reported to be somewhat higher in the postanalytic phase. In a large study of errors detected in blood banks, the distribution was 41% in the preanalytical phase, 4% in the analytic phase, and 55% in the postanalytical phase.⁷

Poor communication^b between laboratory professionals and clinicians is generally cited as the chief issue affecting quality of laboratory services during the preanalytic and postanalytic phases.⁹⁻¹² Throughout the health care system, communication failures are a leading cause of shortfalls in quality, particularly of preventable errors that harm patients.¹³⁻¹⁵ Widely overlooked in training of health care providers is that few clinicians or laboratory professionals receive formal training in effective communications.

Preanalytic communication involves discussion between the clinician and the laboratory to select an appropriate test or set of tests and the communication of appropriate patient information on requisition slips. These communications may involve an extensive set of medical professionals including physicians, nurses, pathologists, medical technologists, laboratory technicians, and clerical staff. They may communicate about test orders, patient identification information, and specimen adequacy. Postanalytic communication entails laboratory professionals' communications with the clinician about critical values and interpretation of laboratory findings. Breakdowns in pre- and postanalytic communication lead to errors, patient safety events, and inefficient and ineffective use of health care resources.^{16, 17}

The next sections review each component of the TTP and provide examples of the types of quality issues and errors that are documented in the literature. In addition, the general discussion of the TTP is followed by a more specific discussion of quality issues and errors associated with POCT. Much of the information is derived from research conducted by CAP through its Q-Probes® and Q-Tracks® studies.

^b Communication is defined as the effective transmission of knowledge or information from one individual to another. It requires clear and concise formulation of data, transformation of the data into useful information, and an agreed method of communication understood by the sender and receiver.⁸

PREANALYTIC PHASE

Clinician Knowledge of Diagnostic Tests

Many laboratory test selection errors arise because clinicians lack adequate knowledge for decision-making when ordering complex testing regimens. Physician knowledge of laboratory tests and ability to order appropriately is complicated by two factors: (1) rapid proliferation of new tests and tests for additional analytes; (2) lack of formal education in laboratory testing. Recent advances in biochemical, molecular, and genetic sciences have led to a plethora of new laboratory diagnostics for clinical use. Currently, there are more than 4,000 different laboratory tests on the market, including new genetic tests that can be used for an estimated 1,430 diseases. Although orders for routine genetic tests and newer assays of increased breadth and complexity are increasing, medical students are exposed to only 29 hours on average of didactic coursework in medical genetics.¹⁸⁻²⁰

Primary care and specialist physicians need to be familiar with broadening sets of existing and emerging screening and diagnostic tests. According to a 1999 survey, 25% of primary care physicians indicated that their medical knowledge base is insufficient for the scope of the care they are expected to provide.¹⁹ Some 38% of specialists believe that primary care physicians cannot maintain adequate expertise to deal with the overload of new clinical information. Even when physicians lack knowledge for diagnostic or management decisions that poses threats to quality or medical malpractice, they only obtain definitive answers to address their uncertainties about 30-50% of the time.²¹ Day-to-day clinician demands leave little time to acquire this intricate knowledge.^{19,20} Continued medical and scientific advancement will compound challenges associated with ordering the optimal sequence of tests, correctly interpreting results, and incorporating genetic information into clinical practice.⁹

Appropriateness of Clinician Test Selection

Definitions of appropriate care vary, e.g., as follows:

- According to IOM, the best care is synonymous with appropriate care and results from the conscientious, explicit, and judicious use of current best evidence and knowledge of patient values by well-trained, experienced clinicians.¹⁴
- RAND has defined appropriate care as that in which the expected benefits exceed the expected risks by a sufficient margin such that the service is worth doing.
- CAP defines appropriateness as the extent to which a particular procedure, treatment, test or service is effective, clearly indicated, non-excessive, adequate in quantity and provided in the inpatient, outpatient, home or other setting best suited to the patient's needs.²²

Principles of appropriateness in laboratory medicine are embodied in selecting the right test at the right time for the right patient. Test appropriateness is inherent to an understanding of the specific clinical condition and the value of a particular test to the respective patient. The ability to make these determinations varies among clinicians. Standard measures of appropriateness do not prevail currently, though their development is viewed as important. Instead, clinical guideline performance indicators of care quality and measures of test use (including underuse and overuse) have been the basis for drawing conclusions about appropriateness. For example, the sentinel

2003 study by McGlynn et al. on the quality of U.S. health care evaluated clinician performance on 439 indicators of quality, 131 of which involved laboratory testing or radiography.²³ Only 61.7% of patients received the recommended laboratory or radiology tests for preventive, acute, and chronic care associated with priority health conditions. The study findings called attention to serious shortfalls in use of key tests that support care quality.

Studies of appropriateness can be undertaken for different applications of laboratory testing, including screening for disease in asymptomatic individuals, establishing a diagnosis in persons presenting with signs and symptoms of disease, and monitoring the course of disease or its treatment. Screening may include panels of laboratory tests performed as part of periodic health evaluations, or tests performed at the time of hospital admission, pre-operative evaluation, or prenatal evaluation. Examples of screening tests include fecal occult blood testing for colorectal cancer, cholesterol testing to detect risk of coronary artery disease, and Pap smears for cervical cancer.^{c,27} Underuse is a common problem for several tests that reduce mortality by early detection of disease or prompting interventions to control risk. The 2006 National Healthcare Quality Report from AHRQ reported that 51.7% of adults over age 50 had colorectal cancer screening in the previous two years (i.e., sigmoidoscopy, colonoscopy, proctoscopy, or fecal occult blood testing), indicating that half of adults in this population are not receiving needed cancer screening.²⁸

Other studies have demonstrated overuse of certain screening tests. For example, while Pap smears are recommended for most women, they are not routinely recommended for women older than 65 or in women following hysterectomy (unless they have previous cervical neoplasia). In 1996, the USPSTF recommended that routine Pap smears are unnecessary in women who have undergone a hysterectomy for benign disease and no longer have a cervix. Yet, based on findings from large-scale U.S. survey data for 1992 and 2002, among women who had ever had a hysterectomy, 68.5% in 1992 and 69.1% in 2002 had a Pap smear within the previous three years of the survey. After adjusting for Pap smears performed prior to a hysterectomy, and hysterectomies that spared the cervix or were performed for cervical neoplasia, the investigators estimated that 10 million women, or half of all women who had undergone hysterectomy, were being screened unnecessarily.²⁹ Still, some clinicians and patients often prefer a cautious approach, especially if neoplasia was present. Other bodies of research show that some screening tests, such as routine admission or preoperative panels of tests, are of limited or no utility.^{30,31}

Monitoring involves testing to track the course of disease, make necessary adjustments in therapy, or detecting complications of care. Examples include testing for HbA1c in diabetic patients and lipid levels in patients with diabetes or known coronary artery disease. According to the 2006 National Healthcare Quality Report, performance rates of monitoring tests for diabetic patients were relatively good. Of adult diabetic patients, about 90% had HbA1c measured in the past year, but only 45.5% had their HbA1c level under optimal control and only 48.1% had their total cholesterol under control.²⁸ While these figures represent an improvement over previous years, improved use of laboratory testing likely would facilitate better control. Of course, measurement alone does not ensure desired outcomes. In a study of more than 1,700 diabetic patients at 30 U.S. academic medical centers during 2000-2002, high annual rates of testing for HbA1c, blood

^c Use of other screening tests, such as glucose testing for diabetes, prostate specific antigen testing for prostate cancer, and thyroid stimulating hormone, testing for thyroid disease, is supported by some groups; however, a strong evidence-base for their preventive value is required by the USPSTF before recommendation.²⁴⁻²⁶

pressure, and cholesterol did not translate to effective metabolic control. Only 40.4% of patients received needed therapeutic adjustments for high HbA1c values.³²

Estimates of diagnostic testing appropriateness are derived mostly from estimates of test use. However, drawing broad conclusions about rates of inappropriate use across tests, settings, and timeframes can be flawed. In a review of 44 eligible reports in the laboratory utilization literature from 1966 to 1997, investigators found that reported rates of inappropriate use ranged from 4.5% to 95%, suggesting significant inconsistencies in the validity of implicit or explicit criteria for appropriateness and reliability of their application.¹⁶ Even for laboratory use among physicians treating patients with the same diagnosis, there is considerable variability.³³ Further research to develop and validate criteria for appropriateness evaluations is needed.

More recent studies using clearly defined algorithms found that, when guidelines were applied, 20-25% of frequently ordered tests, such as autoantibody tests, infectious disease serologic tests, and hepatitis serology tests were inappropriately requested.³⁴⁻³⁶ Redundant test requests also are common and contributed to inappropriate use. In a multicenter CAP study, 1.5% of thyroid stimulating hormone (TSH) requests appeared to be redundant. When applied to high volume testing, even this apparently low rate can result in substantial unnecessary costs. In 2005, an estimated 12.3 million TSH assays were performed at a cost of \$288 million.³⁷ Applying the CAP data, the annual cost of a 1.5% rate of redundant testing is \$4.3 million. A randomized trial of a computer-based intervention to reduce redundant test use found that 1.2% of tests were redundant, but use of computer alerts led to test cancellation of 69% of these redundant tests. Even so, the net impact of the computer alerts was small because less than half of the redundant tests were ordered via computer, only half of the computer orders were screened for redundancy, and almost one-third of the reminders were overridden.³⁸

Physicians often order certain laboratory tests habitually or because they are grouped together for convenience. Multiple factors lead to inappropriate use of tests, including test panels that contain unnecessary tests, delays in performing tests, and difficulties caused by ordering forms or menus.³³ Efforts to decrease utilization and improve appropriateness have focused on changing physician behavior by altering requisition forms, changing policy, instituting computer rules and reminders, and changing reimbursement. Those that target multiple components of behavior modification appear to be most effective.³⁹ For example,

- In a randomized trial conducted in hospitals in France, redesign of laboratory ordering requisitions resulted in higher rates of compliance (83%) to ordering guidelines for thyroid function tests compared to conventional ordering (63%), reducing inappropriate test requests.⁴⁰
- In a time-series study of interventions to improve rates of appropriate testing in non-hospital clinical laboratories in Ontario from 1991 to 1997, the combination of physician guidelines, laboratory requisition form modification, and changes in reimbursement policy for commonly used tests resulted in large shifts in the ordering of certain tests. Specifically, orders decreased for total thyroxine tests by 96%, iron-related tests by 80%, urea-related tests by 58%, erythrocyte sedimentation rate tests by 57%, and TSH tests by 12%, along with increases in certain tests encouraged for substitution.⁴¹
- A computer alert system with basic metabolic panel rules to be applied after hospital admission in a large U.S. academic medical center decreased panel orders by almost

60% without changing patient length of stay, mortality, readmission rates, or transfer rates to ICUs.⁴²

Because laboratory test results help clinicians determine diagnoses, therapies, and need for follow-up tests, inappropriate test use can compromise case management and increase cost per patient and rates of adverse health outcomes.¹⁶

Test Ordering

When a clinician decides to order a laboratory test, a requisition slip (order form) is completed in writing or electronically and submitted with the specimen to the laboratory. Information on the order forms can directly affect processing and analysis of the specimens.

Inaccurate or incomplete requisitions are another source of error and can affect the quality of laboratory testing.⁴³ A CAP Q-Probes study of 577 institutions reported in 1995 that examined how accurately physicians' test orders for inpatients were transmitted to the laboratory found that 97.1% of documented physician orders were completed by the laboratory. However, 1.9% (median) of test orders were not completed and, of the 17,085 patient records examined, 10% were not completed at all. Reasons given as the most likely cause for not completing ordered tests included:

- Failure to enter orders correctly into hospital computer (41.8%)
- Test requisition improperly filled out (12.8%)
- Physician handwriting was unclear (4.1%)
- Failure to enter orders correctly in the laboratory computer (1.4%)
- Other (23.0%) and not applicable (16.9%)

The study also found that the specific laboratory test was not listed on the requisition or in the patient's medical record for 2.5% of the 224,431 laboratory tests performed; this occurred most often in hospitals where verbal orders are more frequent.⁴⁴

Similar findings were demonstrated in anatomic pathology. A 1996 CAP study of surgical pathology specimens reported that missing or incorrect information on order forms accounted for 77% of all deficiencies. Specifically, the most common of these deficiencies was no clinical history or diagnosis (40%). Smaller hospitals and laboratories had more cases with inadequate documentation than larger hospitals. The additional clinical information, when obtained, confirmed the diagnostic impression in 59.4% or was not relevant to pathologic diagnosis in 25.1% of cases. However, the diagnosis was changed substantially in 4.2% of cases and required a report revision in 1.9% of cases.⁴⁵

Computerized physician order entry (CPOE) systems have been promoted as a means of improving the quality of care, reducing errors, and increasing efficiency.^{15, 46-48} Because CPOE systems are complex and costly to implement, efforts thus far have focused primarily on the use of CPOE for medication ordering in hospital settings.⁴⁹ However, a recently published literature review identified 19 studies^d of the impact of CPOE on pathology services from 1990 to 2004.⁵⁰

^d Fifteen studies compared CPOE with and without specific decision support mechanisms and four studies compared setting with and without CPOE systems.

Use of CPOE (as compared to conventional ordering) resulted in statistically significant decreases in the volume of test ordering for blood count, chemistry, serum, and stat tests; when CPOE was linked to additional decision support features, volume decreases ranged from 9.5% (per patient per day) to 45.6% (per hours per patient day). Costs associated with laboratory ordering also decreased by up to 28% for certain tests.

Direct access testing, in which individuals can directly request that certain tests be performed on their own blood or urine specimens, is permitted in 26 of 50 states and the District of Columbia.⁵¹ An additional 12 states permit limited DAT. About 10-15% of laboratories offer direct access testing.⁵² Although these tests are increasingly marketed and used, few data exist on their utilization, appropriateness, accuracy, or impact on consumer decisions or health outcomes.⁵³

Patient Preparation

During the next steps of the preanalytic phase, several factors can affect the quality of laboratory results. Whether at the physician's office, the laboratory, or the patient's bedside, the most important factors include patient preparation and identification and specimen collection and labeling.

Inadequate patient preparation is a common source of misleading laboratory test results.⁵⁴ Preparation factors that may affect laboratory test results are food intake, time of day, exercise, stress, posture, time in menstrual cycle, medications, smoking, and illness unrelated to the condition for which the test was ordered.⁵⁵ For example, accurate glucose determination requires a fasting specimen and tests for drug levels need to be performed when drugs are at steady state. Calculating medication dosages based on inaccurate drug levels can have adverse consequences. In a CAP Q-Probes study reported in 1993 of 666 institutions and more than 18,000 toxic levels, 22-31% of digoxin levels in the toxic range were collected before the steady state of the drug was reached. The investigators found that small institutions, outpatients, stat specimens, and laboratory policies not requiring the time of the last dose before measurement were associated with higher percentages of specimens drawn before the recommended time had elapsed.⁵⁶ Laboratories do not have direct control over these factors, especially when non-laboratory personnel collect samples; however, the laboratory can develop and disseminate information about appropriate patient preparation.

Patient Identification

Patient identification problems are one of the most common causes of erroneous laboratory results.⁵⁷ Quality assurance (QA) and professional organizations (e.g., The Joint Commission) have cited accurate patient identification as a key indicator in patient safety and quality improvement initiatives. Progress with the use of patient wristbands with appropriate identifying information in the hospital setting have been made, though errors can still occur. For example, a study of electronic barcode systems demonstrated their success in reducing and eliminating identification errors for all patients requiring blood transfusion from 1999 to 2002. A portable, hand-held, scan-and-print device was used to verify and document patients' identify at two critical points of transfusion: blood sampling for compatibility and blood administration. In the first three years of hospital-wide use of the device, no incidents occurred of blood transfusion to wrong patients or wrong labeling of blood samples with 41,000 blood sampling procedures and administration of 27,000 units of blood.⁵⁸

A two-year CAP study included wristband errors as a quality indicator.⁵⁹ Continuous monitoring led to significant decreases in wristband errors of all types from 7.4% (mean) at the start of the study to 3.1% (mean) at its conclusion, although at the 10th percentile, there were wristband errors in 11.4% or more of patients. As a percentage of all errors, the most common errors were:

- Missing wristbands (71.6%)
- Missing patient identification information (9%)
- Illegible wristband (7.7%)
- Erroneous identification information (6.8%)
- Conflicting information (3.7%)
- Wrong wristband (1%)

Hospital practices associated with fewer patient identification errors include written protocols governing patient identification, placing new wristbands immediately when needed, and having dedicated phlebotomists collect blood specimens. Laboratories with policies that required phlebotomists to refuse to draw blood from patients with wristband errors reported the fewest specimen identification errors.

Barcode systems have been developed for use at the point of phlebotomy, but little data have been published on their use. In one study, using a beta version of a commercial system reduced error by 77%.⁶⁰ As with computerized order systems, however, use of barcodes may increase certain error types. An evaluation of the Department of Veterans Affairs barcode medication administration system identified five common error patterns, including degraded coordination between physicians and nurses and decreased ability to adapt to changes from routine.⁶¹

Specimen Labeling/Identification

Patient identification problems can easily translate to specimen labeling problems.

Typically, labels are generated and applied to containers prior to specimen collection. Additional labeling and numbering of the specimens may occur as specimens are processed for analysis. Different institutions use different rules for counting specimens. Some assign a single accession number to each specimen, while others assign the same number to all specimens from a single phlebotomy or outpatient encounter, or assign separate numbers for aliquots destined for different laboratory divisions.⁶² In surgical pathology, a single case number is usually assigned to multiple specimens; then, each specimen is assigned a separate specimen identifier in addition to the case number.

Specimen identification errors can result in serious patient injury such as wrong-patient cancer resections and fatal transfusion reactions.^{63, 64} While error rates for individual institutions may be relatively low, those error rates at the national level may yield a significant number of events. For instance, one CAP study reported in 2002 detected specimen-related errors at 0.3% of total errors, of which 5.8% were associated with inadequate labeling.⁶⁵ In a 2006 study of these errors in laboratories associated with 120 institutions (teaching, private, and local hospitals, independent laboratories, federal government facilities), the authors reported adverse events resulting from 1 of every 18 specimen identification errors (5.6%), which, if extrapolated to the nation's 6,000

hospital laboratories, would result in 160,000 events.⁶⁶ Such extrapolations are difficult to validate because of the lack of standardized measurements^e for reporting data in CAP studies and because the laboratories in the studies are not a representative national sample.

Labeling errors have been studied extensively in transfusion medicine, where correct specimen identification is critical to avoiding fatal transfusion reactions. In a study of transfusion errors in New York State, undetected phlebotomy^f errors were the cause of 13% of ABO-incompatibles^g transfusions, while failure to properly identify the patient at the time of transfusion caused another 38% of incompatible transfusions.⁶⁷ An international study of 82 facilities in 10 countries determined that mislabeled specimens (defined as missing some or all identifying information needed for acceptance) occurred in 1 of 165 specimens, while misidentified specimens (in which the blood appeared to be from a patient other than who was identified on the label) occurred in an estimated 1 of 1,986 specimens.⁶⁸

Mislabeled/misidentification of specimens is a common error in anatomic pathology. Errors usually occur when patient or specimen information on containers is missing or inaccurate. For example, specimen-related errors can include misidentification of the origin of the tissue specimen (e.g., stomach vs. colon), anatomic location (e.g., ascending vs. sigmoid colon), and laterality of the tissue (e.g., right vs. left breast).⁶⁹ A 1996 study detected identification and accessioning errors in 6% of more than 1 million surgical pathology specimens. Specimen identification errors accounted for 9.6% of these deficiencies, 77% of which were due to missing or incorrect information. Among the specific deficiencies were:

- Illegible patient name or universal patient identifier (UPI) on either container or requisition
- No label on container
- No patient identification on container
- Patient name/UPI on container does not match that on requisition
- Patient name/UPI on container or requisition does not match master list
- Wrong patient name/UPI on both container and requisition
- No tissue source indicated on container or requisition
- No date of procedure
- No name of submitting physician
- Incorrect information other than patient name/UPI on container or requisition (e.g., sex, age)

Laboratories performing 20,000 or more accessions per year had the highest rate of deficiencies at 6.0% compared to those performing fewer than 20,000, which ranged from 3.2 to 4.5%. Also, institutions that labeled containers with the patient's name and UPI had fewer deficiencies than those that uses either one alone.⁴⁵

^e CAP data collection typically is not standardized with clear definition of a numerator and denominator. Thus, data from each institution may measure indicators differently and may use different detection and reporting criteria.

^f Phlebotomy refers to venous blood drawing.

^g ABO-compatibility refers to the laboratory testing to determine blood type A, B, or O compatibility between the donor and recipient.

Use of relatively new information and communication technology has led to substantial improvements in patient and specimen identification.⁷⁰ Computerized specimen-handling systems include portable data loggers for laboratory personnel, and automatically upload patient and specimen information into the laboratory information system (LIS). Barcode identification systems are being used successfully in more institutions to create standardized labels for laboratory specimens.^{71,72} Errors still can occur when barcoded labels are transferred to the specimen container. The risk of this error is higher in busy emergency rooms or ICUs where multiple labels for different patients may be printed in advance of the specimen collection. Other approaches under evaluation include radiofrequency identification chips and patient imbedded chips.⁷³

Specimen Collection

Clinicians (e.g., nurses) or laboratorians (e.g., phlebotomists) may collect patient specimens. Blood is the most common specimen submitted to laboratories. In CAP Q-Probe studies of phlebotomy,^h reported rates of success (i.e., specimens judged by the laboratory to be suitable for analysis) have been 99.6% among ambulatory patients⁶⁵ and 93.2% among inpatients.⁷⁵ Lower rates have been reported for inpatients because phlebotomists had more difficulty in obtaining specimens (1.6%) or patients were not available (2.3%). Other common types of clinical pathology specimens collected for analysis include urine, cerebrospinal fluid, serous fluids, feces, gastric fluid, and synovial fluid. Anatomic pathology specimens are those obtained by aspiration, washing, smear or scraping for cytologic examination or tissue taken during biopsy or surgery.

As a group, specimen collection problems are some of the more common causes of preanalytic variation and may be associated with failure to collect the correct type of specimen, correct volume of specimen, or collection of an unusableⁱ or misleading specimen. The specimen adequacy often cannot be determined until the analytic phase, when the specimen is assessed for acceptance or rejection. There are limited data on error frequency associated with collection of the wrong type of specimen. A 1997 study of the stat testing section of a university-based laboratory in Italy reported that 2.1% of all TTP errors were attributed to incorrect specimen collection.⁷⁶

Inadequate volume for testing is a common cause of specimen rejection. This problem affects not only blood specimens, but other tests such as Pap smears. In a multicenter study involving 768 laboratories, 0.5% (median) of Pap smears had inadequate specimen volume and another 5.8% (median) had adequate volume but limited the ability to evaluate the specimen for cervical cancer due to other specimen-related factors.⁷⁷ Two studies evaluated specimen rejection for complete blood count (CBC) and chemistry specimens. Of 703 hospitals, 0.45% of CBC specimens were rejected; 10.1% of rejections were due to insufficient specimen quantity.⁷⁸ The subsequent 1997 study of chemistry specimens reported that 0.35% were rejected prior to testing; of these specimens, 11.4% were rejected due to inadequate volume.⁷⁹ In the stat testing study mentioned above, specimen volume and adequacy for analysis were affected when phlebotomy was performed from a patient's infusion; this inappropriately diluted the specimen volume in 20.6% of cases.⁷⁶

^h Most medical and laboratory professional are trained to collect blood specimens but a specialist in this area is the phlebotomist.⁷⁴ Blood specimens can be collected from various sources. Venipuncture and phlebotomy refer to collection of blood from veins, while skin puncture refers to collection from capillaries. Arterial blood also is collected for blood gas measurements and pH.

ⁱ An unusable specimen is generally due to trauma during its transport that results in hemolysis or clotting.

To ensure that specimen volume is sufficient for testing, laboratories often recommend specimen volumes that exceed those needed for testing. Several studies noted collection of up to 45 times the amount of blood actually needed for testing, raising concerns about production of “iatrogenic anemia” in high risk hospitalized patients (e.g., ICU patients, neonates, elderly) who undergo repeated blood collection.^{80,81} The decisive factor contributing to blood loss was rigid blood drawing schemes in which repetitive drawings were performed regardless of the patient’s clinical condition.⁸² Reporting of individual cumulative blood loss on the daily laboratory report may influence the requesting clinician’s behavior. Earlier studies examined the use of a pediatric collection container for adult patients, which led to a 50% reduction in the mean daily blood loss; however, this change had no effect on the ordering clinician’s requests for laboratory tests that were not medically necessary.^{83, 82, 84}

Unusable (e.g., due to hemolysis, clotted blood specimens) or mislabeled specimens are the most frequent reasons for specimen rejection. Proper specimen collection and labeling is essential for hematology and coagulation testing, where attention to specimen quality is necessary for an optimal laboratory result.¹⁷ Several studies reported that hemolysis^j of chemistry specimens caused 54-60% of specimen rejections and occurred five times more frequently than the second-most cited reason of insufficient volume; clotted specimens caused 65% of CBC specimen rejections.^{5, 78, 79} Among rejected chemistry and CBC tests, a higher percentage were collected in pediatric microcollection tubes.

Contamination of specimens collected for bacterial culture is another common source of error, estimated at 2.5% of positive blood cultures and 18% of urine cultures in reports published in 2007.^{85, 86} Because it can be difficult to distinguish a false positive from a truly positive culture, patients with contaminated cultures are often given unneeded care, increasing hospital costs by thousands of dollars per patient.⁸⁷ Similar contamination rates have been reported in inpatient and outpatient specimens.⁸⁵ Continuous monitoring, use of dedicated phlebotomists, feedback to those drawing specimens, and use of faster acting decontamination techniques all reduce the frequency of contaminated cultures.⁸⁸⁻⁹¹ There are many other sources of error in microbiology testing, including wrong type of specimen collected for type of infection, insufficient specimen collected, contamination of specimen collection containers and solutions, and poor timing of specimen collection and transport.⁹²⁻⁹⁴ When microbiology specimens are collected during a surgical procedure, contamination of surgical blades also may cause errors.⁹⁵

Health care and laboratory settings also can affect specimen collection. In a recent study comparing rates of and reasons for specimen rejection across different settings as well as associations with patient demographic factors, of the 0.74% of specimens that were rejected, 47% were from the inpatient setting, 27% from the emergency department, and 25% from outpatient setting. After adjusting for the total number of specimens per site, the emergency department rejection rates were twice as high as rates for inpatient services and five times as high as rates for the outpatient setting. Also, the rejection rate of specimens from African Americans was twice that of the rates for Caucasians and 30% higher than the rate for other races in the hospital setting but indicated no difference in the outpatient setting.⁹⁶ The investigators hypothesized that the severity and seriousness of the diseases and comorbidities of patients admitted to emergency department or inpatient services are contributing to the higher proportion of specimens rejected.

^j Breakage of red blood cells membranes causing the release of hemoglobin and other internal components into the surrounding fluid.

In general, African American patients are more likely to choose the emergency department as the mode of entry to the system, independent of health insurance status, therefore increasing the likelihood of errors.⁹⁷

Specimen Delivery

Specimen quality can be compromised during delivery by excessive delay, adverse temperature, or manual or mechanical trauma to the specimens.⁵⁵ Different means have been employed to transport specimens to and within the laboratory, such as human couriers, pneumatic-tube systems, and other technologies, that have advantages and disadvantages. For example, using human couriers is a “batch process” dependent on pickup at specific times.⁹⁸ While reliable, it entails significant training and management costs. Pneumatic-tube systems (i.e., tube transport systems that move contents via vacuum and positive pressure) provide cost-effective, rapid transport for specimen delivery in hospitals.⁹⁹ Evidence on potential for specimen damage from acceleration and deceleration forces is mixed. Although some evidence suggests that mechanical factors – tube length and speed, and number of times transported – may result in hemolysis of blood specimens,¹⁰⁰ other evidence shows no clinically significant effect of these systems on hematology and coagulation results.¹⁰¹ Other technologies such as track vehicles, mobile robots, and conveyor belts are now widely used to transport specimens from one point within the laboratory to another. Although safe to specimens, transport via these technologies tends to be slower. Implementing all of these technologies entail capital expenditures for installation and costs for transition from old to new systems, training, and maintenance.

Each specimen type has standards for timely delivery and conditions for transport in order to maintain its integrity. Specimens for stat orders such as those collected in an emergency room need to be delivered to the laboratory immediately. Most microbiologic organisms die quickly after removal from the body and should be transported quickly. Specimens for some tests (e.g., cryoglobulins, cryofibrinogen) need to be kept at body temperature, while others need to be protected from light (e.g., bilirubin, vitamin A).^{74, 102} Transporting and processing delays can render a specimen invalid for analysis. For example, a 2000 study of one-hour delays in the processing of blood samples found significant effects on the concentration of biomarkers. Decreases in the concentrations occurred for red and white blood cells, high-density lipoprotein cholesterol, glucose, and creatine. Increases in concentration were observed for total cholesterol, total testosterone, free testosterone, alkaline phosphatase, total bilirubin, and thiobarbituric acid-reactive substances.¹⁰³

CLINICAL PATHOLOGY TRANSITIONAL PREANALYTIC

Specimen Processing and Preparation

Once received, the laboratory processes the specimen for analysis. Quality in processing requires that the laboratory verify specimen labeling (e.g., patient identification, time of collection, initials of sample collector) and information provided on the accompanying requisition (e.g., patient identification, tests ordered, relevant clinical information).⁷⁴ Pertinent information must be accurately transcribed and logged manually or entered into the LIS. Specimens may arrive at the laboratory with a barcoded label generated at the point of specimen collection. Next, the specimen is evaluated according to guidelines on its acceptability for analysis. Accepted

specimens are distributed to specific laboratory sections for analysis or additional preparation (e.g., centrifugation). If a specimen is rejected, another must be obtained, increasing the cost of care. Specimens that cannot be tested immediately and those tested only during certain days/shifts are stored appropriately (e.g., refrigeration or freezing).

Quality problems in specimen processing (aside from patient misidentification described above) include transcription errors and forwarding the wrong specimen type. Transcription presents opportunities for multiple types of error. A study published in 1999 reported that 4.8% of outpatient requisition slips had at least one laboratory order entry error type, including discrepancies in the test ordered, physician's name, and test priority status.⁴³ Order entry errors tended to be higher in facilities with a greater percentage of occupied hospital beds, those that made extensive use of verbal orders (in person and by telephone), and federal facilities in both urban and rural settings. In contrast, an Australian study of pathology laboratories reported in 1996 found transcription error rates of up to 39% among lowest performers and up to 15% among best performers.¹⁰⁴ Error types in order of prevalence included those related to patient and physician identification, patient sex and age, tests requested, and patient ward location or address. Transcription errors can be decreased through routine rechecking of orders entered against requisitions and substitution of verbal orders with written and facsimile orders.^{43, 105, 106}

The evaluation of specimen suitability is a critical factor in test result accuracy, precision, and usefulness. Preanalytic problems (e.g., specimen collection) may not be discovered until the examination for acceptance. Accepting unsuitable specimens can lead to erroneous information that compromises patient care.¹⁰⁷ Guidelines for evaluating specimens are integral to QC procedures, and rates of and reasons for specimen rejection are evaluated as an indicator of quality. The high rates of acceptance of inadequate specimens resulting in incorrect Pap smear interpretation with subsequent adverse effects on patients in the late 1980s precipitated increased regulation of the laboratory sector. It also helped to prompt development of new technology to aid in detection of abnormalities. Proceeding with microbiology or other testing of specimens of insufficient volume may result in false-negative blood cultures, adversely affecting antibiotic management. As mentioned, leading reasons for rejecting specimens often are associated with problems in the preanalytic phase, including hemolysis, improper method of collection, empty specimen container, mislabeling of container, clotted specimen, delay in transport, and significant platelet clumps.¹⁰⁸

When accepted, specimens undergo additional preparation for analysis. Preparation of clinical pathology specimens involves several activities: centrifugation,^k aliquoting,^l pipetting, diluting, and sorting specimens with appropriate labels (often barcoded) into batches for introduction into automated analyzers or other methods of analysis.¹⁰⁹ Molecular testing methods have the potential to replace many conventional microbiology laboratory assays.^{110, 111} Preparation of microbiology specimens for these new molecular-based testing methods may involve nucleic acid purification and amplification with automated systems instead of manual procedures. Studies of resource allocation demonstrate that specimen preparation consumes a large portion of the laboratory budget (19%) and staff time (37%), and exposes laboratory workers to the risks of

^k Centrifugation is the use of a mechanical device that uses centrifugal or rotational forces to separate substances of different densities, such as solids from liquids or liquids from other liquids.

^l Aliquoting is the separation of an equal fractional part from the whole, especially specimens of substances that have the same volume or weight.

handling infectious specimens.¹¹² In addition, specimens requiring separation by centrifugation historically have been bottlenecks in laboratory processes because of the time required to manually load and unload the instruments.¹¹³ The introduction of automated preanalytical processing systems has reduced labor, hazard, and errors associated with specimen processing.

In larger laboratories, preanalytic processing systems often are linked directly to analytic systems, forming total laboratory automation systems whereas in other, usually medium and smaller laboratories, they operate as modular or stand-alone systems. Because these systems can include instruments for chemistry, immunoassay, hematology, coagulation, drug screening, and other tests, they allow for dramatic gains in consolidation of work and personnel and the integrity of specimen handling.¹¹⁴ Preanalytic processing units typically perform the basic tasks of reading barcodes, centrifuging specimens when required, and decapping and sorting tubes, as well as more complicated tasks such as checking the quality of a specimen with instruments designed to detect substances that interfere with testing, such as hemoglobin, bilirubin, and lipoprotein levels.¹⁷ Some units have capabilities for postanalytic storage and retrieval. Most importantly, these systems eliminate much of the rote manual work of laboratory staff that causes errors due to fatigue or distraction.¹¹⁵ In a recent evaluation of an automated preanalytical blood specimen processing unit at two U.S. academic health centers, sorting and routing errors decreased from 7,950 to 477 per month and biohazard exposures decreased from 2,658 to 6 per month.¹¹³

CLINICAL PATHOLOGY ANALYTIC PHASE

Specimen Analysis

Along with preanalytic activities, the quality of test results depends on factors linked to the analytical systems or processes used for testing itself. In clinical pathology, many tests are conducted using automated laboratory instruments that analyze the specimen and generate results. Technologies include, but are not limited to, chemistry analyzers; immunoassay instruments; hematology, coagulation, and urinalysis equipment; electrochemistry,^m electrophoresis, chromatography, mass spectrometry, and flow cytometry instruments; and molecular diagnostic technology.¹¹⁷ Although some analyzers require more operator involvement than others, in general, high levels of automation have enabled laboratorians to concentrate more on QA and results interpretation.¹¹⁸ In addition, most laboratory QC and assurance programs have targeted accuracy and precision during specimen analysis. As a result, the risks and rates of testing errors have been significantly reduced to the extent that analytic systems now have the lowest error rates when compared to any step in the preanalytic and postanalytic phases.¹¹⁹ This trend is expected to continue given recent advances in technology development supporting connections between analytic systems and preanalytic processing units to create total laboratory automation.

The overarching goal of analytic system quality is to ensure run-to-run accuracy and precision (i.e., reproducibility). Accuracy is the degree of conformity of a measured or calculated quantity to its actual, nominal, absolute, or some other reference value. Precision refers to the closeness of agreement between independent test results obtained under prescribed conditions; it is a measure of reproducibility or random error. Achieving accuracy and precision requires

^m Electrochemistry involves the measurement of current or voltage generated due to the activity of specific ions. Several different types of instruments are used for these measurements.¹¹⁶

careful selection of reagents, rigorous use of controls, and strict adherence to established protocols. While automated analytic systems have successfully minimized many errors, factors such as interference and calibration can alter the conditions of measurement, create variance and/or bias, and diminish accuracy and precision of testing systems, results, and interpretation. A 2001 report of a CAP survey of PT specimens for therapeutic drug monitoring that evaluated 25 drugs among 5,000 laboratories found that 57.8% (range 35.3-73.7%) of variance was due to long-term, within-laboratory variance, 25.0% (8.8-50.6%) was due to short-term within-laboratory variance, and 17.3% (5.0-35.4%) was due to between-laboratory variance; total laboratory variance was 82.7% (64.6-95.0%).¹²⁰

Bias, or systematic error, refers to the extent to which a measurement, sampling, or analytic method systematically underestimates or overestimates the true value. Analytic bias can directly affect patient classification and clinical decision-making by shifting the distribution of test values.¹²¹ For example, a major study examined the relationship between matrixⁿ effects and the accuracy of laboratory measurements for 11 analytes, based on CAP Comprehensive Chemistry Survey data for 1994, and using definitive methods at the National Institute of Standards and Technology and CDC. Among the findings were that matrix biases affected results in 69% test comparisons and that, because of matrix biases, the reference value was the correct target value only 32% of the time. Other error was introduced by random matrix effects and calibration biases.¹²² Minimizing bias is accomplished by examining contributors to variance in test values including sensitivity and specificity, interference, instrument calibration error, reagent lot differences, personnel performance error, and other factors.¹²³⁻¹²⁵

A common cause of bias is interference, which is caused by specimen components other than the analyte that influence the concentration measurement.¹²⁵ Interference may be caused by a single, identifiable substance or property of the material. Major endogenous sources of interference include hemoglobin, lipemia, bilirubin, and proteins and extraneous antibodies, while exogenous sources include drugs, materials given to patients for diagnostic purposes, and additives from collection containers (e.g., anticoagulants, preservatives).¹²⁵ Interference can lead to falsely elevated or lowered measurements. A 2002 study of 5,310 patients in the UK for whom common immunoassay tests for TSH and/or gonadotropins were requested found that, of the instances of interference in immunoassays for TSH, luteinizing hormone, and follicle-stimulating hormone, the interference was large enough in 82% to cause inaccurate results and have potentially adverse effects on patient care and health care costs.¹²⁶ The magnitude of interference can vary significantly. Whether or not the bias due to interference is clinically significant depends on the use of the test results and the allowable error rate. In general, laboratorians are guided by the allowable error rates given in the criteria for acceptable performance in PT specified in the CLIA regulations.

Other causes of bias that can result in spurious test results include instrument calibration error, reagent lot differences, inaccurate mathematical correction for specimen dilution, and misinterpretation of instrument codes.^{123, 124} Calibration is a measurable signal related to a substance concentration or other reported result. It requires testing the specimen against one or more materials (calibrators) that behave similarly to the specimen and for which the true result is known (i.e., a comparator). The response should be linear over the reportable range (i.e., the response should be proportional to the analyte concentration). Calibration drift is a systematic

ⁿ A matrix is the biological medium such as blood, urine, or breath in which a substance is being detected or that is being used for a reference standard.

change in measurement that occurs over a time period of unadjusted, continuous operation of a test instrument. In 2004, the National Institute of Standards and Technology released a report on the impact of calibration error in clinical decision making and health care costs.¹²⁷ This report studied calcium results in about 89,000 Mayo Clinic patients during 1998-1999 and found that calibration error in measurements of serum calcium levels led to analytic bias in 15% of tests results. Not only were some test results passing decision thresholds specified in practice guidelines, but estimated costs of the errors on a national scale were substantial, ranging from \$60 million to \$199 million per year. Similarly, in a study reported in 2000 of inaccurate test results based on data from the New York State Department of Health PT program to characterize the quality of toxicology testing, calibration drift was cited as the most frequent cause of analytic error (48%), followed by method bias (14%), indeterminate source (11%), reportable range (9%), and component failure (8%). This study also noted that approximately half of laboratories used an allowable error for QC of analytic systems that exceeded the threshold error specified by manufacturers for stable instrument performance.¹²⁴ Nonconformity is documented to be highly correlated with process complexity.¹²⁸ There has been a growing trend to have all laboratory measurements traceable to a primary method of analysis reference material, but this may not always be possible when the material being analyzed is unstable.

Lot-to-lot variations in the manufacturing of calibrator and reagent concentrations or volume can lead to bias affecting analytical performance.¹²⁷ The lack of uniformity and standardization among manufacturers makes the implementation of laboratory-based guidelines difficult because each such guideline must have method-dependent decision limits.^{123, 129} The heterogeneity of test values also makes it difficult to integrate data or test results into a patient's medical record, or to make use of the test results outside the institution or setting in which they are produced. This issue is widely recognized in the laboratory medicine sector and efforts are underway to standardize values. Certain tests, such as C-reactive protein, require higher sensitivity in order to correlate test values to clinical diseases (e.g., cardiovascular disease). Efforts to define performance criteria for such high-sensitivity tests may lead to improved standardization, performance in quality assessment schemes, and enhanced risk prediction.¹³⁰

Report Review, Interpretation, and Verification

Subsequent to specimen analysis, the next step in testing is report interpretation and verification. In most large clinical laboratories, test results are produced from and stored in the LIS. In these laboratories, test data may be entered manually into the LIS or automatically transferred to the LIS from automated systems. However, smaller laboratories, POLs, and providers using POCT devices often document values without use of an LIS. In these instances, the results reports may be generated from a printer linked to analyzers or a POCT device, or documented directly in the patient's medical record.

Review of laboratory reports requires checking the results for any instrument error codes, markedly abnormal (especially critical) results, or specimen integrity issues; comparing multiple results on the same specimen if applicable; and determining appropriate commentary for inclusion in the final report. Most laboratories have a few levels of review depending on the type of test and values in the report.¹³¹ At the first level, the technician or technologist analyzing the specimen reviews the test results. Then, the supervisor (technologist) approves results for certain tests, and may report results to the clinician unless additional review by more senior professional

staff is required. At the next level, a professional staff member (e.g., pathologist, doctoral-level scientist, microbiologist, biochemist, bioanalyst) reviews and approves the test results for release. Senior level review and approval usually is performed when test results indicate abnormal values. Manual review of results is necessary in such instances as verification of anatomic pathology results and critical test results. However, automated verification systems now exist for tests such as chemistry and hematology assays.

Most laboratories continue to use manual processes for report validation. Manual test validation is a time-consuming, tedious process with large interindividual variation that slows laboratory TAT.¹⁰⁷ Common errors associated with manual processes are data entry/transcription errors that account for about 4.6% of all hospital laboratory errors.^{43,76}

Automated verification (or autoverification), shows promise in validating results without review when the results meet predefined criteria.^{132, 133} These mechanisms rely on knowledge-based techniques such as internal consistency checks, delta checks,^o and checks for specific errors in addition to the standard reference range and pathological limit checks of the LIS.¹³³ Also, report processing by these systems is fast and highly efficient. For example, an immunoassay autoverification system, under the direction of a supervisor, can validate close to 500 results in about 30 minutes.¹³⁵ Autovalidating can allow senior level laboratorians to focus on difficult cases and interact with clinicians. Some autoverification systems lack the ability to scan control data before the report is generated.¹³⁶ Beyond these advantages, it remains to be demonstrated that autoverification systems improve patient safety and outcomes.¹⁰⁷

Reference Intervals

Reference intervals, also known as reference or normal values,^p are pre-determined values against which laboratory test results are compared in order to allow clinicians to make physiological assessments, medical diagnoses, and management decisions.¹³⁸ The intervals are established by testing a group of individuals selected on the basis of well-defined criteria.¹³⁹

The most common type of reference interval, health-associated intervals, is derived from a reference sample of people who are in good health. For example, 95% of the healthy adult population tested by many laboratories has a serum potassium level that is between 3.5 and 5.1 mEq/L; this range is used to define the serum potassium reference interval. Disease-associated intervals, sometimes referred to as decision-based intervals, are specific medical decision limits that allow clinicians to classify patients as having a disease, as being healthy, or to otherwise manage patients.¹⁴⁰ For example, hyperlipidemia guidelines typically recommend diet and exercise to lower cholesterol in otherwise healthy adults once their serum cholesterol level exceeds a certain threshold, e.g., 200 mg/dL.¹³⁸ Disease-associated intervals are often defined during clinical trials and incorporated into the medical literature and adopted by laboratories.

The creation of reliable reference intervals is an important task for both clinical laboratories and for manufacturers of diagnostic tests. While individual laboratories independently may obtain

^o A delta check is a comparison of consecutive values for a given test in a patient's laboratory file used to detect abrupt changes, usually generated as a part of computer-based QC programs. If a delta exceeds its threshold, the value for "today" fails the check and is suspected of being erroneous.¹³⁴

^p The term reference interval is preferred over normal values because it can be defined for a given reference population.¹³⁷

similar test results, these results may be interpreted differently if different reference intervals are being employed, leading to differences in what is considered healthy or pathological.¹⁰⁹ However, reference intervals historically have been poorly defined and not determined using a uniform process, leading to considerable variation in clinical laboratories.¹³⁹ Inter- and intra-laboratory differences in preanalytic and analytic factors also have been implicated as sources of variation in the development and application of reference intervals.¹⁴⁰

Some work has been done to standardize the reference interval process. CLIA requires that laboratories introducing an unmodified, FDA-cleared or approved non-waived test system verify that the reference intervals supplied by the manufacturer are appropriate for the laboratory's patient population before reporting patient test results.¹⁴¹ CLIA also requires that laboratories modifying FDA-approved tests or developing their own tests establish reference intervals for their assays prior to reporting patient test results. In all cases, reference intervals must be included in laboratory reports or made available to individuals who order tests.¹⁴² In 2000, the Clinical and Laboratory Standards Institute (CLSI) published a voluntary standard for clinical laboratories and test manufacturers that provides information on defining and determining reference intervals with the intention of achieving a level of reliability and accuracy across reference intervals.¹³⁹ Assay harmonization also has been proposed to eliminate the requirement that each laboratory establish its own reference intervals.¹⁴⁰ At present, however, there are few enforced regulations to ensure the validity of the reference intervals defined by individual laboratories. A 2007 CAP Q-Probes study of 163 laboratories found that approximately half of all laboratories adopted reference intervals from manufacturers without testing them on-site using healthy individuals.¹³⁸

For many laboratory tests, no single reference interval applies to everyone because the test may be affected by factors such as age and sex.¹³⁷ For instance, the concentration of alkaline phosphatase, a cellular enzyme responsible for creation of bone, rises in proportion to the production of new bone cells. While children and adolescents should have high alkaline phosphatase levels, high levels in adults can be indicative of disease. Similarly, hemoglobin and hematocrit both decline naturally as part of the aging process. In many cases, reference intervals that are appropriate for pediatric populations and elderly populations have not been widely developed. Thus, test values that are considered healthy compared to aggregate reference intervals may be abnormal if age-specific intervals are used.¹⁴⁰ The 2007 CAP Q-Probes study described above also found that few laboratories test healthy children to establish pediatric reference intervals; most of the laboratories that do test healthy children use in-laboratory testing only to validate reference intervals supplied by manufacturers rather than to establish their own reference intervals.¹³⁸

ANATOMIC PATHOLOGY TRANSITIONAL PREANALYTIC

Specimen Processing/Accessioning and Preparation

Anatomic pathology tissue processing/[¶]accessioning, preparation, and examination in the analytic phase are generally more labor-intensive than for clinical pathology, which, in many large laboratories, relies more on automated modules for analyzing specimens. The exception is microbiology, which also relies on labor-intensive microscopic examination. Some of the

[¶] Accessioning refers to the process of recording and assigning a surgical pathology identifier number to a case and specimen(s) that meet the laboratory's acceptance criteria.

processing tasks of anatomic pathology are analogous to those in clinical pathology. When specimens arrive, information from requisition slips and orders must be accurately transcribed and entered into the LIS or retrieved from a computer-based system designed for anatomic pathology; a sheet of labels is created, the specimen and labels are forwarded to the appropriate pathology section, and the specimen undergoes gross examination for acceptance or rejection. The similarities between processing in anatomic and clinical pathology end there.

Preparation of an anatomic pathology tissue specimen is a complex, multistep process in which the tissue is repeatedly cut, transferred, and relabeled. After initial preparatory cutting, the tissue is embedded in wax to create blocks for sectioning from the gross (whole) specimen and produce slides for examination under a microscope. Most tissue cutting is performed manually by trained professional histotechnologists or pathologists' assistants with the use of a microtome blade or scalpel, though automated cutting systems are in early development. Though infrequent, injuries to the laboratorian can occur during early stage specimen cutting. Usually, such injuries can be avoided by complying with safeguards such as use of protective gloves, use of handles with cutting blades, and avoidance of inherently dangerous maneuvers.¹⁴³

There are many points along the anatomic pathology workflow where errors and other threats to quality can arise.⁶² The most prevalent problems during the preparatory steps involve patient or specimen identification errors and mix-ups, cognitive errors in the gross room, tissue cutting- or staining-related issues, and specimen defects. As noted above, patient and specimen identification errors that affect the analytic phase can begin in the preanalytic phase as a result of incorrect information on the patient or specimen requisition slip, specimen placement in an incorrectly identified container, specimen mix-ups and incorrect test ordering at the time of log in, or transcription errors.⁴⁵ In a broad study of identification errors and mix-ups in all three phases of the testing process for surgical pathology, investigators found numerous sources of identification error, many of which pertain to specimen accessioning or preparation of tissue blocks and slides, including:

- Specimen accessioned to wrong patient in the laboratory
- Case misidentified in the gross room and dictated with wrong accession number or wrong specimen number
- Specimen placed in or embedded into incorrect cassette
- Specimen sections mixed up in water bath
- Specimen placed on slide labeled for another specimen
- Incorrect permanent label affixed to slide
- Incorrect history/paperwork associated with slide⁶²

Additional identification-related errors that take place during and after microscopic examination are listed in the next section.

Cognitive errors can occur during preparatory gross room tasks or microscopic examination. Little detailed information is available about these types of error.¹⁴⁴ An example of a cognitive error of omission, defined as the failure to perform pertinent ancillary studies at the tissue, block, or slide level, may be the failure to take fresh tissue for flow cytometry or the failure to perform a

culture. Other cognitive errors in the gross room may be inaccurate examinations with poor descriptions (e.g., lack of appropriate measurements), lack of or incomplete lesional sampling, and lack of sampling of pertinent areas necessary for proper lesional characterization or staging. Cognitive errors associated with gross room tasks can be common though difficult to detect. However, there is virtually no evidence on rates of cognitive errors in the laboratory.

Incorrect conclusions can be drawn from poor technique associated with tissue cutting (i.e., undercutting or overcutting specimens) and tissue staining (e.g., misidentification of the appropriate stain, incorrect selection of reagents and staining protocol). Cross contamination by “floaters” (i.e., foreign tissue fragments carried over from other sections or specimens) is a better documented quality problem. In a 1996 CAP study of 275 laboratories, extraneous tissue fragments were found in 0.6% of 321,750 slides examined prospectively and 2.9% of 57,083 slides examined retrospectively. For the prospective study, 59.4% of the contaminants were found on slides, 28.4% on paraffin blocks, and 12.2% were undocumented. In comparison, for the retrospective study, 72.9% of contaminants were associated with slides, 15.9% with paraffin blocks, and 11.2% were undocumented. The majority of extraneous tissue came from different cases (63.2% in the prospective study and 48.5% in the retrospective study). Study findings confirmed that more than 92% of instances of extraneous tissue originated in the laboratory.¹⁴⁵

ANATOMIC PATHOLOGY ANALYTIC PHASE

Microscopic Specimen Examination

In anatomic pathology, microscopic examination is the primary method for making clinical diagnoses, although innovative, automated technologies are increasingly being developed and used in cytology and molecular pathology.¹⁴⁶ Digital microscopes with advanced capabilities for taking, storing, replicating, and cataloging digital images are used widely among laboratories.¹⁴⁷ Certain microbiology tests also rely on microscopic examination.

Histotechnologists and cytotechnologists play an important role in the microscopic examination of tissues. They formulate and document interpretive conclusions for presentation of cells, biochemical components, tissue vascularity and, if applicable, presentation of disease, which may include definition of grade and stage of disease, tumor type, measurements, and characteristics.¹⁴⁸ These laboratorians also play an important role in the examination of infectious agents present in tissue specimens. Once the result is approved by the technologist, the pathologist reviews the findings. A secondary case review may be undertaken or required as part of a QC check or if the diagnostic findings are unclear, as discussed further, below.

Because of pathology’s dependence on visual association, technologists and pathologists must possess the cognitive and interpretive skills needed to evaluate accurately tissue specimens and establish diagnoses beyond a reasonable doubt. The skill set requires visual pattern recognition of cells and structures, recognition of whether the arrangement is normal or abnormal, association of the features to diseases that mimic the pattern, development of multiple hypotheses or differential diagnoses, and investigation of the clinical or histological possibilities to rule-in or rule-out diagnoses.¹⁴⁹ In surgical pathology, cognitive and interpretive skills are applied to histologic grading and staging, considered the most important prognostic indicators. Although several grading systems exist, the National Cancer Institute’s three-grade system based on histologic

type, tumor necrosis, and mitotic activity serves as the general standard for determinations. Similarly, the American Joint Committee on Cancer pathologic staging system is the standard to guide evaluations of tumor size and depth. For gynecologic cytology, standards for examination have been codified in CLIA.

QC, performance evaluation, and test reproducibility to minimize diagnostic discrepancies and errors have been more easily defined and applied in clinical pathology than in anatomic pathology.¹⁵⁰ The reliance on subjective judgment and somewhat variable diagnostic thresholds between individuals limits reproducibility and may introduce bias in areas of cytology and surgical pathology. For example, one study conducted in 1995 in the area of neuropathology found discrepancies between general pathologists and neuropathologists. The pathologists were in disagreement in 42.8% of cases. Of those cases, 20.6% were considered serious (e.g., tumor diagnosis changed to non-tumor, diagnosis changed within benign or malignant), 44.9% were less serious but substantial (e.g., glioma type or grade changed), and the remaining 34.6% were minor (e.g., tentative or doubtful diagnosis confirmed). These differences can have detrimental effects on patient management and costs.¹⁵¹

When errors occur in anatomic pathology analytic processes, they can be classified as either cognitive or identification/clerical. Cognitive errors at the microscope include slips and lapses while analyzing slides, poor cognitive formulations, knowledge problems, communication problems (e.g., poorly worded or unintelligible reports), and difficulties in using classification models that have poorly defined criteria. Correct patient and specimen identification and record keeping throughout the processes associated with microscopic observations and documentation are crucial to quality and accuracy.¹⁷ Examples of identification and clerical errors include: pathologist examines wrong slide, pathologist dictates/writes incorrect case number, transcriptionist types diagnosis for incorrect case or specimen; downtime/temporary medical number updated incorrectly, and report prints with wrong patient identifier due to LIS error.⁶²

A literature review published in 2004 reported wide variability in anatomic pathology errors, ranging from less than 1% to 43% (with mean error rates of 1%-5%) among institutions participating in the studies reviewed.¹⁵² Error rates tended to be higher in cytology compared to surgical pathology, with false-negative diagnosis as the greatest source of error. Most cognitive and identification/clerical errors are discovered before sign-out, although a small percentage are discovered thereafter. Discovery in either regard may be precipitated by receipt of additional information or material for the current case or a different recent case, results review by the pathologist or other laboratorian, or pathologist-initiated external consultation with an expert.⁶⁹ Other methods of detection include intradepartmental review or a double-read of the results before sign out, and preparation for or presentation at a conference with clinicians (e.g., board review) after sign-out. The patient's clinician also may question the pathologists' diagnosis and request re-evaluation of the specimen and/or findings, at which time an error may be discovered.

Results Review

In general, laboratory test results are transcribed into the LIS or another computer application, reviewed and approved by the pathologist, and delivered to the clinician. In certain instances (e.g., a difficult case), the pathologist may seek an external consultation with another pathologist for a second opinion or specific expertise prior to finalizing the report. When an experienced

pathologist finds that immediate recognition of the pathologic process does not occur, and that applying familiar rules and criteria do not lead to a clear diagnosis, the pathologist may face an unfamiliar scenario and can be prone to the same types of errors as the novice.^{17, 153} As such, seeking consultation is based on self-knowledge of one's limitations and the severity of consequences of error.¹⁵⁴ A study published in 2002 reported findings on the rates and characteristics associated with expert consultation. Consultations were sought for 0.5% of cases, of which 52% were sent to nationally known experts and 32% were sent to local experts. Among the consultations, 54.6% confirmed the original diagnosis. The referring pathologist's assessment of possible diagnoses was correct in only 21.5% of cases, 15.9% of consultations confirmed the original diagnosis but added significant information, 6.5% were discordant with the original diagnosis, 1.4% were attributed to unidentified other factors, and 0.7% were ambiguous and not helpful.¹⁵⁵

After report sign-out, discrepancies and errors can be detected through secondary case review, e.g., via conference review (such as an oncology board) or institutional review. The specific methods employed to determine discrepancies are correlation of findings and assessment of amended reports. In general, rates of discrepancy and errors after cases are signed out are relatively low for cytology and surgical pathology. One study involving 74 hospitals reported variability in rates and causes of laboratory discrepancies in anatomic pathology. While 10% of hospitals reported no discrepancies, another 10% reported errors in at least 5% of diagnoses. The mean frequency of laboratory discrepancies was 6.7%. About 47.8% of discrepancies resulted in a change within the same category of interpretation (e.g., one tumor type was changed to another), 20.9% resulted in a change across categories of interpretation (e.g., benign diagnosis was changed to malignant), 18.5% were from typographical errors, 9.1% were from a change in patient information, and 3.7% were from a change in margin status. According to the investigators, 5.3% of discrepancies had a moderate or marked effect on patient care.¹⁵⁶

The most common method of detecting errors, before and after sign-out, is through the correlation of findings between different tests on the same tissue specimen. Correlations of frozen-permanent sections and of cytologic-histologic findings are well-documented in the literature. For gynecologic cytology, correlation of cytologic and histologic findings is mandated by CLIA. Discrepancy rates using correlation are generally low. For example, in a hospital study published in 2002, investigators reported discrepancies in nongynecologic cases of 2.26% for cytology and 0.44% for histology, and in gynecologic cases of 0.87% for cytology and 7.37% for histology.¹⁵⁷ These rates were consistent with error frequency rates of other studies. Several CAP studies that examined diagnostic errors on frozen sections also published discrepancy rates in the range of 1.4-1.7%.^{158, 159}

Error rates and types have been assessed by calculating the rate of reports that must be amended. In a large CAP Q-Probes study conducted in 1996 of surgical pathology in 359 laboratories, the aggregate rate of reports amended to change clinically significant information was 1.9 per 1000 cases.¹⁶⁰

POSTANALYTIC PHASE

The main components of the postanalytic phase focus on results reporting and interactions between laboratorians and clinicians. The core challenges for pathologists and other laboratory professionals in their communication with physicians concern timeliness of reporting, notification of significant abnormal test results, and presentation of relevant information through reports and interpretive comments. Customer satisfaction surveys have found that all of these factors receive high percentages of below average and poor ratings.¹² These challenges are often cited as the chief concerns in the postanalytic phase.

Test Turnaround Time

The timeliness with which test results are delivered is one of the most prominent parameters of laboratory medicine and a common indicator of performance.^{161, 162} Common among these are test TAT and time for notification of critical results. Automation of various steps in the analytic phase, increased use of electronic results reporting, and development of automatic electronic alerting systems for critical values have helped to decrease TATs.

TAT is typically assessed by determining the difference between recorded starting times (test ordering) and ending points (test reporting time).^{163, 164} Some laboratories also analyze intervals that comprise TAT, such as test order to specimen collection, collection to laboratory specimen receipt time, and receipt time to reporting time, in order to determine the specific points at which delays occur.¹⁶⁴ A few laboratories also are expanding the scope of measurement by evaluating "therapeutic TAT," the time from initiation of the test order to the implementation of clinical decisions (e.g., change in treatment).¹⁶⁵

Regardless of method, TAT is viewed as a quality measure that reflects the performance of the testing process as a whole. Prompt and predictable reporting of test results can increase efficiency of patient care and improve clinician and patient satisfaction, even when it does not affect health outcomes.¹⁶³ Actions taken as a result of regularly monitoring TAT and other factors may improve certain aspects of performance.^{162, 164} However, researchers also recognize that shorter TAT measurements do not necessarily indicate superior service.¹⁶² That is, absolute measurements of TAT do not reflect whether the laboratory services meet the expectations of the clinicians using those services. Also, improving TAT can be challenging, not only because of the contributing factors outside the control of the laboratory, but because laboratories frequently try to improve TATs for a specific test, location, or specimen type by immediately identifying and assaying those specimens in question, thereby extending the TATs of other tests.¹⁶⁶

Most TAT studies have focused on inpatient and emergency care settings, though a few researchers have ventured to outpatient settings. TAT varies depending on the location of the laboratory (e.g., satellite laboratories often have shorter turnaround times than central laboratories) and the analyte (if other variables stay the same). Typical TAT for routine testing in the emergency setting is 12-48 minutes or less, particularly if POCT is available, a few hours for general testing in the inpatient setting, and a few hours to the next morning or 24 hours for testing in the outpatient setting. One study of stat laboratories for the emergency department and ICUs evaluated outlier^r test TATs,

^r Outlier events are test TATs that exceed targeted or tolerable reporting times. These events are used to assess the degree to which laboratory services meet the needs of clinicians.¹⁶²

accounting for about 10-15% of total events. The majority of problems directly affecting TAT for selected chemistry tests are associated with preanalytic-related test ordering and specimen collection (57%) and analytic-related personnel and technical problems (28%).¹⁶⁴ Staff shortages in both phases were the major cause of delays. The percentage of delays was 4.7% higher in ICUs than emergency departments. Shortened TATs have been associated with rural locations, delivery of specimens as collected, pneumatic tube delivery systems, and continuous versus batch testing.¹⁶⁷ Innovative POCT devices also have had a significant impact of the reduction of TAT. For example, a study of stat TAT in an academic health center reported TATs that were 1-2 minutes shorter for bedside testing compared with a satellite laboratory and 9-12 minutes shorter in the satellite laboratory compared to the central laboratory.¹⁶⁵

Data from studies of TAT for outpatient testing in hospital laboratories has produced different results. In 1997, a Q-Probes study of TAT for three common assays reported that 50% of laboratories were able to verify 90% of results within 2.7 hours for the CBC, 3.5 hours for the biochemical profile, and 21.6 hours for TSH.¹⁶⁸ For half of participants, outpatient testing accounted for about 46% of the typical hospital laboratory workload. A follow-up study reported in 2002 found increases in TATs to 3.9 hours for the CBC, 4.9 hours for the biochemical profile, and 38.1 hours for the TSH.¹⁶⁹ TATs increased for specimens received later in the day for all analytes and when specimen transport was not under the control of the laboratory.

TAT, laboratory practices, and specimen characteristics (e.g., type of specimen and findings) associated with anatomic pathology (e.g., cytology, surgical pathology) have been examined as well. Result availability and timeliness are considered indicators of quality for anatomic pathology. Turnaround times varied substantially according to specimen type. A study of gynecologic cytology found that 50% of laboratories had a mean TAT of 6 days or less, though the average laboratory could complete 90% of their cases within 8 days; 10% of laboratories needed 13-19 days.^{s,170} TATs for nongynecologic cytology (e.g., fine needle aspirations) are much shorter; 50% of laboratories had a mean TAT of 1.6 days or less (3 days for 90% of cases); 10% needed 3.2-6 days.¹⁷¹ These cytology studies found that longer TATs were associated with the need to contact the physician's office for additional information, and use of students, residents, or fellows in the evaluation. In addition to these factors, gynecologic cytology TATs were influenced by use of reference laboratories for all or part of the evaluation and provision of service on the weekend, whereas TATs for other cytologic specimens were influenced by issuance of atypical/suspicious findings for malignancy diagnosis; having to pull prior case material for review; having to perform cell blocks, special stains, or other activities; and not having transcriptionists working weekends.

Many laboratories also monitor TAT for surgical pathology with the goal of having the majority of cases signed out within 1-2 days.¹⁷ A 1995 Q-Probes study of biopsies and complex specimens documented mean TATs of 1.5 days for complex cases, 1.3 days for routine cases, and 2.6 days for cases requiring special handling.¹⁷² Factors associated with increased TAT included: institutional bed size greater than 450, responsibility for gross section dissections assigned to residents only, slides not available to pathologist before 12:00PM, resident involvement in sign-out, interposing a day between availability of slides and final sign-out for resident education purposes, and a greater number of pathologists on staff. These findings were confirmed in a subsequent study

^s They concluded that, if one week is acceptable TAT and actual screening time is 5-10 minutes per slide, there is room for improvement.

published in 1998. Pathologists had signed off on 85.9% of biopsy diagnoses by the second working day, and surgeons received the hard-copy reports by the fourth working day.

Notification of critical values/test results

A critical value or test result represents a pathophysiologic state at such variance with normal as to be potentially life-threatening unless something is done promptly and for which some corrective action can be taken.¹⁷³ Timely, if not immediate, notification of critical values or results is crucial to patient safety. Regulatory bodies now require laboratories to have policies for notification of such values, although performance benchmarks and definitions of specific critical values can vary by accrediting organization, laboratory, or health care setting.¹⁷⁴ In many instances, providers will order laboratory tests even though the patient is not in a life-threatening pathophysiologic state.

The variance may be in the high and low limits of the analyte values.¹⁷⁵ In 2002, a CAP study of 623 institutions confirmed wide variation in critical values for routine chemistry and hematology tests, with no value being the same in 80% or more of laboratories.¹⁷⁶ For certain common analytes (e.g., glucose, potassium, hematocrit, white blood cell count), almost all laboratories had high and low critical values. For other analytes, laboratories had either a high or low critical value. About 72% of laboratories did not have a policy on repeat critical values for the same patient. Of particular note is that more than 45% of critical values were unexpected and 65% resulted in therapeutic change.

The Massachusetts Coalition for the Prevention of Medical Errors and the Massachusetts Hospital Association are leading a state-wide initiative to standardize critical values and reporting mechanisms for laboratory, cardiology, radiology, and other diagnostic tests across all health care institutions.¹⁷⁷ The initiative aims to address “errors in the process of communication of test results that are both frequent and have the potential for serious harm.” A set of safe practice recommendations has been developed to promote successful communication of test results. In addition, the group established a standardized set of abnormal test values widely agreed to be critical to patient health.

The limits chosen for any clinical result directly affect the institution’s workload, as notifying clinicians of critical values is labor intensive. A CAP Q-Probes study of 623 institutions, published in 2002, found that telephone contact is the primary method of reporting critical values by more than 90% of laboratories, with calls taking an average of 6 minutes for inpatients and 14 minutes for outpatients. The calls were made by the laboratorian performing the test, most often a technologist. For certain types of tests, other methods of notification include facsimile, computer, and voice mail.¹⁷⁶

Misreading values is not the only problem of communication. In hospitals, accrediting organizations have required communication only with the responsible physician or caregiver (usually a nurse) since 2000. To minimize miscommunication of values during notification calls, The Joint Commission requires the receiving clinician to “read-back” the critical value along with patient identifiers.¹⁷⁸ They also recently added monitoring of TAT for critical value reporting as a measure of quality and patient safety.

Previously, communication followed CLIA provisions, which permit reporting with the entity or individual ordering or responsible for using the results, including unit secretaries. This is

still the case in the outpatient setting. Nurses receive 65% of reports in hospitals and unit/clerical staff receive the largest percentage (40%) of reports in physicians office practices.¹⁷⁶ Communication with clerical staff instead of clinicians can result in another type of error – undocumented critical values in the patient’s medical record.¹⁷⁴ Lastly, some critical values result from preanalytic problems, such as with specimen collection or analytic interference, rather than medically significant values.¹⁷⁹

While critical results in clinical pathology are time-sensitive, anatomic critical values are typically viewed as information-sensitive in that the report content is highly important but usually does not require immediate action.¹⁸⁰ Occasional diagnoses in surgical pathology and cytology require immediate notification of the clinician to rapidly initiate treatment.¹⁸¹ Guidelines for critical results reporting in anatomic pathology have not been established. Consequently, there is a wide range of opinion among pathologists about the need for an immediate telephone call and the degree of urgency. Furthermore, most anatomic pathology results are not quantified with values and limits. A 2004 study examined the potential for developing parameters to address critical results in surgical pathology and identified 11 possible cases including, but not limited to, renal biopsy specimens, vasculitis, and bacteria in heart valves or bone marrow.¹⁸² Differences in opinion prevail; only 58% of these reports documented calls to the clinician. There was a greater difference of opinion when a new metastasis was identified in a patient and when an organism was identified in an immunocompetent patient.

Report Formatting

Laboratorians are trained to convert valuable data to useful clinical information in the form of laboratory results reports – the major communication link between laboratorians and clinicians. The reports are communicated to the clinician most often with the assumption that the basic pathologic process described is understood correctly. While the clinician’s level of experience and training has direct impact on their understanding, this is not always the case, particularly with growing use of genetic tests and microbiology tests. Yet, little attention has been focused on educating and training clinicians to more fully understand pathology reports.¹³ Few published studies have evaluated comprehension of laboratory reports and, of those available, most focus on anatomic pathology.

The content, format, and physical presentation of the information significantly affect the interpretation and use of laboratory data by clinicians.^{76, 183} Mistakes in the content and completeness of laboratory reports as well as misunderstanding by the treating physician as to the significance of the information in the report, among other factors, can delay treatment of a serious disease and alter outcomes.¹⁴⁴ Problems can be magnified when a critical result is unanticipated by the clinician.

Specific report content issues can include any of the following: uninterpretable information, incorrect data or reference intervals, inaccurate patient identification, or incorrect physician or patient location for reporting results. A 1992 CAP study of mistakes in clinical pathology laboratory reports found that the frequency of content errors was lowest in blood bank reports, intermediate in chemistry and microbiology reports, and highest in hematology reports.¹⁸⁴

Clinicians’ limited willingness or ability to interpret laboratory reports may result in their focusing inordinate attention on certain values while disregarding others of potential importance

or failing to discern broader clinical implications. For example, in a survey of attending and house staff physicians in a major hospital system reported in 2002, only 4 of 11 analytes routinely reported in the CBC battery were selected as frequently or always useful by more than by 90% of responding physicians: hemoglobin, hematocrit, platelet count, and white blood cell count. Primary care physicians also chose mean cell volume as a useful parameter in the evaluation of anemia. The investigators suggested that modifications to report formats were needed to facilitate physician perceptions of the importance of hematology laboratory results.¹⁸⁵

Laboratories also must be cognizant of how new medical findings affect results interpretation and reporting. The incorporation of new evidence into clinical guidelines can expand indications for treatment, requiring laboratories to update report content and interpretations. For example, in 2001, the U.S. National Cholesterol Education Program issued new guidelines for the prevention and management of high cholesterol in adults, based on accumulated evidence concerning the contribution of lipoproteins (and other risk factors) to the development of coronary heart disease.¹⁸⁶ The guidelines necessitated changes in laboratory analyses, reporting, and interpretations including: modification of cut-points, standardization of measurements, fasting profile at initial screening, and testing for emerging risk factors and secondary dyslipidemias.¹⁸⁷ Values must be presented clearly in reports with appropriate interpretive comments reflecting current guidelines.

Several organizations have developed voluntary minimum standards outlining the data elements that should comprise reports. For example, CMS endorsed the Bethesda System for reporting cervical cytology results, CDC issued standards for reporting HIV results, CLSI has suggested standards for microbiology test results and others, CAP established several standards for specific types of clinical and anatomic pathology reports, and the Association of Directors of Anatomic and Surgical Pathology has focused on its respective areas of expertise.

The data elements for reports are selected with the primary aim of promoting accuracy and completeness. The different standards are widely accepted; however, variability in report accuracy and completeness remains among laboratories. For example, a CAP Q-Probes study of bladder biopsies and curettings in 268 institutions noted that the presence or absence of muscularis propria should be routinely included in reports of all biopsies. Yet, for invasive carcinomas, definitive assessments were reported in only 53.3% of cases, and in only 30% of noninvasive carcinomas.¹⁸⁸ Another CAP study of breast biopsies, published in 1997, found that 23% of reports of malignant cases were missing information on tumor size, 17% on tumor grade, and 8% on margin status, and 24% did not have information on the extent of intraductal carcinoma.¹⁸⁹ These studies and others also found that the single practice that was most effective in ensuring completeness of reporting was use of a checklist. The checklist guides laboratorians in documenting test results to ensure the inclusion of specific data in the final report.^{189, 190}

The physical presentation of test results can influence the clinician's understanding of them.⁸ Poorly designed reports can result in misunderstandings and/or undervaluation of important information.¹⁹¹ More specifically, the spacing, highlighting, font size, and formatting of content can affect comprehension of computer-generated reports for clinical and anatomic pathology. Grammar and word selection also are important for anatomic pathology reports where, unlike clinical pathology reports, results are documented via selection of predefined phrases and drafting of free text commentary. In general important, unusual, or critical results in clinical and anatomic pathology reports can be emphasized with capitalization, a special mark in the margin, or

underlining.¹⁹² Color highlighting in electronic reports or printouts can highlight a result for the viewer's attention. Unfortunately, most computer-generated reports still crowd data into columns on each page, are single-test focused, and employ limited use of graphics for certain tests.^{123, 193}

Because specific details of interest to the user are more difficult to abstract from sentences and paragraphs, clinical and anatomic pathology reports now organize content in synoptic formats.¹⁹⁴ Key information provided in tabular form is generally a reproduction of the checklist data. Variable amounts of free text can be added in the form of special gross features and comments on other important findings and implications. In general, the data elements are relatively consistent from one computer program to another, but the presentation may differ according to vendor. Laboratorian selection of data elements also may result in content differences. Synoptic formatting generally has improved report legibility relative to straight textual summaries, although more work is needed to ensure timely comprehension of test results and accompanying information.

A few researchers have examined the impact of redesigned report formats to more graphically-oriented models.¹⁸³ One recent study of surgical pathology reports assessed the effect of report redesign on physician comprehension and found a 30% discordance rate between pathologists' intended meanings and interpretation by surgeons.¹⁸³ The authors stated that stylistic improvements have the potential to interfere with comprehension and increase the number of misunderstandings, and that further research is needed. Generally, researchers believe that the forthcoming proliferation of proteomic and genomic tests will challenge clinical informatics and prompt changes to existing report formats.¹⁹³ To meet this challenge, the next generation of laboratory reports must make better use of graphical displays to facilitate the rapid assimilation and comprehension of important data. Developers have been using these concepts to improve the design, function, and comprehensibility of electronic health records (EHRs) over the last decade. Further advancements should incorporate user-friendly graphical displays of laboratory data.

Physician Interpretation and Follow-up

In the TTP, a laboratory test is not complete until its result has been interpreted by the clinician and incorporated into patient care, as appropriate. There is considerable evidence indicating that, for a variety of reasons, physicians often do not take, or do not document, appropriate actions in response to abnormal laboratory test results. In a CAP Q-Probes study of elevated calcium levels in 525 institutions, published in 2000, 3.5% of reports of abnormal levels were not entered into patient medical records. Of reports that were entered, 23% did not contain physician progress notes responding to elevated calcium results; this figure rose to 93% for patients with no known history of hypercalcemia. Also, follow-up tests were not ordered for 13.8% of the elevated values. However, in a follow-up survey of physicians for whose patients there was neither physician documentation of an abnormal test nor ordering of the designated follow-up test, the majority of responding physicians indicated that they did order the test and that the results led to further action that was not documented in their notes.¹⁹⁵ A retrospective study of 2000-2002 data in 30 U.S. academic medical centers reported that only 40% of diabetic patients with high HbA1c and only 5.6% with high low-density lipoprotein cholesterol had adjustments in treatment based on these results.³² A similar study of 1999-2000 data of elderly non-insulin-requiring diabetics in Ontario showed that fewer than half of the patients of endocrinology specialists or primary care providers had adjustments in treatment based on elevated HbA1c levels.¹⁹⁶

Interpretive Consultation Services

The actual and potential benefits of laboratorians providing information and consultation to physicians on laboratory test selection and interpretation of patient-specific results is generally recognized.^{10, 197, 198} While most laboratories provide some form of interpretive comments in anatomic pathology reports, this is not always the case with clinical pathology reports. Medicare reimburses consultations only for the 20 clinical pathology tests that frequently require interpretation by a pathologist.¹⁹⁹ Most private insurers and managed care organizations follow this Medicare policy.

The primary barrier to interpretive commenting is the shortage of true experts with high subspecialty expertise in clinical pathology. Other barriers contributing to this problem include: generally low reimbursement for professional activities within clinical laboratories; more complex criteria for reimbursement of selected clinical pathology tests; and a shift toward the practice of anatomic pathology where reimbursement for interpretive comments is provided for all anatomic pathology tests.^{197, 199} As a consequence, most current pathologists and scientists do not provide clinically valuable interpretations in areas such as coagulation, autoimmunity, and other complex areas of laboratory medicine, although some of these professionals do so despite lack of incentives. A 2004 report of an evaluation of interpretive commenting in clinical chemistry found that many of the comments were automatically generated by a computer, whereas others were individually generated depending on the results and availability of clinical information. The majority of comments were acceptable; however, some comments were inappropriate, misleading, or, in few instances, dangerous to patient care.¹⁹⁸ Inappropriate comments were the result of inaccurate assumptions by staff when the clinical information available was insufficient or when the expertise in clinical chemistry subspecialty areas (e.g., toxicology, endocrinology, and tumor markers) was inadequate.

Despite these few challenges to interpretive commenting, the service generally is well received by physicians.^{10, 12} Several organizations have been studying methods of improving the quality of communication between clinicians and laboratorians during ordering and results interpretation by developing programs that expand the use of interpretive commenting in combination with other tools. For example, a major academic medical center instituted a broad laboratory medicine interpretive service and undertook a series of studies to assess improvements. The service provides a physician expert-written, evidence-based, patient-specific interpretation that accompanies the results of complex laboratory testing panels.^{9, 197} A study of its coagulation service found that 98% of physicians perceived the interpretations as useful or informative, 59% perceived reduced time to diagnosis, 72% perceived that the interpretation reduced the number of laboratory tests required to make a diagnosis, and 72% believed that it helped them to avoid misdiagnoses.¹⁰

POINT-OF-CARE TESTING

POCT, also known as bedside, near patient, decentralized, or alternative site testing, refers to clinical laboratory testing that is conducted close to the site of patient care outside of the traditional, core, or central laboratory.^{200, 201} The main objective of POCT is to produce a result quickly, facilitating decisions about appropriate treatment and care to improve clinical or economic outcome.²⁰² POCT can be performed in various settings, including sites of primary care (e.g., physician's office and community clinic, community pharmacy, health center, workplace

clinic) and secondary and tertiary care (e.g., emergency room, ICU, outpatient clinic, ambulatory diagnostic and treatment center).^{t, 203}

Similar to traditional laboratory testing, POCT can be delineated by preanalytic, analytic, and postanalytic components.^{204, 205} Some benefits of POCT include decreases in the amount of specimen required and minimization of delays that are associated with specimen transport, processing, and preparation²⁰³

Ensuring high quality in POCT poses several challenges. Many POCT devices are granted CLIA-waived status and are operated by personnel whose primary training may not be in the clinical laboratory sciences and who may, therefore, be unfamiliar with testing practices.^{202, 206} Unlike laboratorians in the central laboratory, POCT operators often have minimal time to reflect on the TTP and may not have access to ancillary information such as QC data. Non-adherence to test protocols and procedures and operators' use of reagents that are not controlled are two other sources of error in POCT.²⁰⁴ Improved QC performance in POCT blood glucose monitoring has been directly associated with supervision of QC programs by laboratory personnel rather than nursing personnel.²⁰⁷

Laboratory experts have also identified possible sources of POCT error amplification, i.e., conditions that increase the frequency or likelihood of POCT error, including those that become preventable adverse events.²⁰⁴ For example, suboptimal use of real-time POCT results, such as initiating the incorrect therapeutic action or failing to immediately recognize the significance of a test value, can amplify errors in POCT. While the immediate availability of POCT results can significantly enhance the quality of care, additional research is needed to determine the best methods for integrating POCT into day-to-day clinical processes (i.e., care pathways).²⁰⁸

PREANALYTIC PHASE

Selection of Testing Method

In the hospital setting, professional laboratory consultation and inclusion of the laboratory in the selection of test methods and ongoing management of POCT are important components of successful POCT programs.^{209, 210} Consultations with the core laboratory can assist clinicians by providing information about the advantages and disadvantages of POCT versus core laboratory testing in specific patient settings.²⁰⁵ Laboratory participation in the development of practice guidelines for laboratory order sets can decrease practice variability and ensure that POCT operators are following the most cost-effective pathway to the best patient outcome. Laboratory staff also can create reference manuals for each nursing unit (or physician office) that contain written procedures, policies, training checklists, and other information.²⁰⁵

Testing in physician offices differs considerably from that conducted in the hospital setting, particularly in such matters as testing menus and knowledge of quality-related procedures. Physician office personnel usually have been trained only in performing a few tests of limited complexity.²¹¹ If questions arise pertaining to POCT, these personnel typically contact the diagnostics manufacturer rather than consult with a hospital or independent laboratory.

^t While certain POCT can be conducted at home by individuals, this chapter focuses on clinical uses of POCT; home laboratory testing and direct access testing are discussed elsewhere in the report.

Test Ordering

Excessive or incorrect test ordering can contribute to medical errors at the point of care.^{204, 208, 212} Excessive ordering can confuse and overwhelm test interpreters. Increased use of CPOE, clinical decision support systems (CDSSs), and EHRs may prevent incorrect, excessive, and redundant POCT ordering by standardizing test ordering and reminding clinicians about previously ordered laboratory tests.^{38, 213, 214} CPOE and CDSSs are discussed in greater detail in the Laboratory Information Systems chapter of this report.

Another source of error related to test ordering is mistimed or uncoupled testing, which occurs when the delivery of laboratory test results is not synchronized with the therapeutic intervention during dynamic treatment.²⁰⁴ For example, if incorrectly timed or interpreted, receiving results of POCT pH and bicarbonate tests during infusions of bicarbonate for patients undergoing cardiopulmonary resuscitation may prompt test interpreters to react to test results stemming from a transient or recent pathophysiological state, rather than to the patient's current state.

Patient/Specimen Identification

POCT error patterns related to patient and specimen identification tend to differ from those that occur during traditional laboratory-based testing. Patient misidentification is more likely with POCT in emergencies when there is a greater potential for a staff member dispatched to perform POCT on a patient to mistakenly test or record results for a different patient.²⁰⁴ POCT operator entry of an incorrect patient identification number can lead to such problems as posting of results to the incorrect patient medical record, inappropriate medical treatment, and unavailability of POCT results for comparison with previous and subsequent test results.^{204, 205} Incorrect patient identification also can result in failure to post test results in the LIS and improper billing.

Patient identification errors in POCT can be reduced. Computerization of POCT devices increasingly allows for electronic capture of information such as the date, time, operator and patient identification, device serial number, reagent and control lots, and control ranges, thereby automating this information capture.²¹⁵ Some POCT devices have mechanisms that lock out operators who repeatedly make identification errors, facilitating corrective counseling of these operators prior to further use.²⁰⁵ For example, one health system that implemented a "three-strike rule" found that glucose meter testing errors decreased significantly, although there was no impact on the rate of blood gas errors.²¹⁶ Other POCT devices can lock out testing if patient identification is invalid or unavailable.²¹⁷ Another method for safeguarding hospitalized patients prior to POCT includes cross-checking patient information against the bed location.

Electronic barcodes have been installed in hospitals recently to automate data entry, and many POCT devices have built-in barcode scanners.²¹⁸ In order to be successful, all of the components that must be identified to the system must be barcoded, including the patient, operator, testing strips, and QC materials. Following implementation of an automated barcoding system, one health system found significant reduction in error rates in the glucose and blood gas devices.²¹⁶ Another example of barcoding is a POCT system that uses a special syringe with a unique barcode identifier that scans the barcode, the patient's wrist band, and the phlebotomist's identification badge.²⁰⁸ In this system, the patient's identification is maintained throughout all phases of testing and is linked to the test results and other relevant information. However, limitations in barcoding (e.g., difficult to read through blood stains and moisture, limited number of encodable characters, need for proper

physical alignment of barcode and reader) have prompted interest in other systems for automatic identification, including radiofrequency identification.²¹⁸

A POCT error that is characteristic of outpatient settings results from batching of specimens.²⁰⁴ This error most often occurs with urine tests and rapid tests for GAS antigen that are left on the counter. Labeling of containers and swabs immediately upon collection reduces batching-related errors.

Specimen Collection

Specimen collection errors include inappropriate or inconsistent specimen type, volume, or application to the testing surface or reaction chamber on the POCT device.²⁰⁴ Operator variability and error rates in POCT specimen collection are influenced by several factors, including the extent and effectiveness of operator training and the frequency with which POCT operators perform specific tests and progress along the learning curve for each test.²⁰⁴ Several approaches can be employed to reduce the likelihood of specimen collection error. For example, minimizing the number of different types of POCT devices and the number of staff performing testing and selecting a single manufacturer and model of device for hospital-wide use allow for using one testing protocol and training program, resulting in less confusion for POCT operators who work at several sites.²⁰⁵ Operators also need to be trained and revalidated. Several studies have reported that non-laboratory professionals can obtain measurements that are just as accurate as those obtained by laboratory professionals if properly trained in QA and device maintenance prior to using the POCT device.^{219, 220}

Automation in POCT devices can prompt the operator to enter specific information, ensuring that every test follows the same sequence.²⁰⁵ Some POCT devices have functions that warn the operator about common preanalytic errors and lock out untrained operators.

ANALYTIC PHASE

The relative importance of precision and accuracy in POCT depends on the site of testing. For home-use POCT, precision is likely to be more important; while a POCT device may be biased, the device is functional as long as the patient knows how to track and interpret results over time and determine treatment based on the results generated by that device.²²¹ In those circumstances, absolute accuracy is not as important as the precision and daily consistency of results. Whether they are evaluated in an emergency room, operating room, ICU, general medical unit, or outpatient setting, the results of POCT must correlate closely to those generated by the central laboratory via results verification, including delta checks, and interpretation.

An important POCT issue concerns the tradeoffs between rapid results and analytical test performance.²⁰³ Several studies have assessed the analytic validity of POCT devices, primarily comparing POCT results to those obtained in the central laboratory. Findings vary by the setting of device use. For example, two recent studies confirmed the precision and accuracy of POCT glucose meters using blood samples from patients attending outpatient clinics for routine checkups and who were not suffering from underlying disease that required immediate hospitalization.^{222, 223}

A study investigated the performance of POCT glucose meters in hospitalized patients with serious underlying disorders in addition to their diabetes found that, at high and low glucose

levels, there was significant disagreement between glucose meter readings and laboratory analyzer readings. The authors concluded that clinicians should be cognizant of POCT meter readings at the hypo- and hyperglycemic levels and corroborate these results with those obtained by central laboratory analyzers whenever possible.²²⁴ Another study measured the accuracy and clinical impact of three common POCT methods for glucose measurements in critically ill patients receiving insulin infusions: glucose meter analysis of capillary blood (finger stick); glucose meter analysis of arterial blood; and blood gas/chemistry analysis of arterial blood.²²⁵ All patients were enrolled for a maximum of three days and had at most nine sets of measurements. Glucose meter analysis of arterial and capillary blood tended to provide higher glucose values than blood gas/chemistry analysis of arterial blood. The study reported that the magnitude of these differences led to frequent clinical disagreements regarding insulin dose titration in insulin infusion protocols for aggressive glucose control.

Specimen Analysis

Several factors can interfere with the operator's ability to detect factors that can degrade POCT test quality. Most POCT assays accept small sample volumes, in which evidence of hemolysis (i.e., the breakdown of red blood cells) or clots can be difficult to detect. Some POCT devices now contain a mechanism to detect the presence of clots or bubbles in the specimen.²⁰⁵ Common errors also result from patient-related interference (e.g., non-specific agglutinins in precipitation slide tests), specimen-related non-target influences (e.g., drugs that cause false results in chemistry POCT devices), and specimen-reagent combination-related matrix effects.²⁰⁴ The design of most POCT devices hides specimen reaction sites from view, making it difficult or impossible for the operator to assess the progress of the reaction or to distinguish patient, specimen, and matrix sources of error.

Another opportunity for error in the analytic phase of POCT arises from failure to calibrate a POCT device, deviating from the calibration protocol, and misrecording calibration data.²⁰⁴ Similar to all laboratory instruments, calibration requirements for POCT devices differ depending on such factors as how frequently the device is used and whether it is disposable after single use. Among other requirements for non-waived POCT devices, the CAP 2006 checklist requires that calibrators for POCT devices are properly labeled, calibration results are documented, criteria are established for calibration verification, and test systems are recalibrated when calibration verification fails to meet the established criteria.²²⁶ The CAP checklist for waived POCT requires calibrators to be properly labeled and that POCT programs follow manufacturer instructions for calibration and calibration verification.

Quality Control

Because central laboratory and POCT methods and techniques differ, traditional QC applied to POCT can be costly and ineffective for identifying problems that can compromise the quality of POCT results.²²⁷ It is difficult to apply conventional QC procedures to POCT for several reasons, including: the number of different instruments, the diverse training and experience of POCT operators, and the inability to view and assess the analytic reaction chamber of the devices.²²⁸ Some laboratory experts contend that QC is irrelevant and unnecessary in POCT because the instruments are relatively error-free and the prevalence of preanalytical errors renders QC of the analytical process useless.²²⁹ However, most experts believe that POCT must have a QA and QC

program equivalent to those used in the central laboratory. The latter position is supported by the findings of the CDC Pacific Northwest Monitoring Network study, which reported that 42% of POCT waived tests were regarded as providing a definitive diagnosis without further confirmation and 9% were used to monitor patients and whose results had the potential to directly affect therapeutic interventions.²³⁰

The design of POCT devices, particularly those for single-use testing, has forced manufacturers to assume responsibility for building QC into POCT products, a process often referred to as “autonomation.”^{208, 229} Increasingly, if the instrument-controlled analytic process fails to meet the manufacturer’s quality criteria, the patient’s data are not released, thereby allowing the manufacturer to guarantee a statistically defined level of quality associated with each test result.²⁰⁸ Internal QC systems may encompass electronic checks to assess the performance of the instrument’s electronic circuits, temperature, sample flow, electronic stability, and sensor response.²³¹ Built-in basic positive and negative controls (i.e., “test worked/test failed”) are capable of assessing the viability of the analytic testing process, and more sophisticated, quantitative measurements can provide numerical responses to the analyte concentrations in the control. More advanced systems may include a series of integral liquid controls and calibrators contained in closed reagent packs that have been validated by the manufacturer.²⁰⁸ Also, POCT devices may automatically record QC data, producing charts and statistics and applying QC algorithms to the data.²³¹

In addition to these built-in QC functions, other forms of POCT QC are recommended. Specifically, POCT operators should directly observe instrument or method function by performing and recording results of QC testing each day.²⁰⁴ POCT supervisors should observe operators performing and recording QC and quiz operators on various scenarios of QC failure. For both operators and supervisors, checklists help to ensure that procedures are being followed. Instrument or worksheet records can be compared to patient or maintenance records to identify any inconsistencies in the transfer of information.

Laboratory experts agree that a QC check must be performed following the initiation of a new batch of reagents and when the system is recalibrated.^{u,203} Many experts also suggest that QC be performed when each sample is run and when each new operator uses the system. Methods to determine the frequency of QC testing often are based on factors such as the overall analytic performance and reproducibility of the system and the number and competence of the operators. Typically, the frequency of QC depends on the type of POCT device. For bench top analyzers, QC may be run at least once per shift (i.e., three times per day), whereas for critical care analyzers, QC can be preprogrammed to occur at specific intervals.

Failure to perform QC has been cited as a common problem among facilities using POCT.²³³ CAP Q-Probes studies demonstrated that POCT operators commonly neglect to perform QC and/or report patient test results, even when QC procedures do not follow specified control guidelines.²³⁴ Several studies have examined optimal QC techniques for POCT used in a variety of medical settings. A large university-based health system studied nearly 600 technicians and nurses who had verified competency to perform POCT using two different devices to measure blood gas, chemistry, and hematocrit levels. In this study, reported in 1999, investigators compared POCT results and core laboratory results extracted from the LIS and from POCT data management

^u CLIA requires that operators of waived tests follow manufacturers’ QC directions.²³²

stations. Discrepancies were noted and changes were implemented to improve POCT reliability where problems were identified, including in-service training and provision of additional POCT equipment. The investigators concluded that POCT processes could be monitored and corrected using continuous quality improvement techniques.²²⁷

A similar study involved a formalized continuous quality improvement program in which all testing sites in a large medical center were reviewed on a monthly basis for quality indicators such as QC and maintenance performance, PT, patient identification, and alert value confirmations.²³⁵ Major aspects of quality improvement requiring attention included instrument maintenance documentation, QC documentation for manual tests, and documentation of actions taken with the correction of failed QC tests. Significant improvement was made in QC documentation of urine dipstick testing, including that the number of POCT sites not documenting more than 5% of QC results was reduced from 30% to 15%.

Another facility's QA program involved a database designed to incorporate five main components:

- Documentation of initial device performance and reagent/control lots
- Documentation of operator competence and compliance with daily QC regulatory requirements^v
- Storage of proficiency and patient correlation results
- Monitoring of performance and policy compliance
- Determination and documentation of the effect of POCT on patient outcome using links between the POCT database, EHR, and LIS²²¹

Drawing from a national survey and consensus process reported in 2001, a multidisciplinary group of experts in critical care POCT programs and other hospital disciplines determined that QC in POCT must involve a mechanism for blocking patient testing if required QC procedures are not performed.²¹⁷ These experts also recommended that requirements for QC and QC timing be matched to clinical priorities, patient test results be suppressed if QC results are unacceptable, exceptions to QC procedures be recognized for emergency situations, and that decisions be made about when to implement routine, urgent, or critical interruptions to QC processes.

Result Generation and Verification

Because POCT data are generated in series, operators often are not afforded a real-time review of trends and deviations in the sequence of test results that could enable identifying possible errors.²⁰⁴ Whereas delta checks of routine and stat central laboratory testing tells whether a patient's laboratory test result differs significantly from previous results reported with the same assay, POCT operators do not usually have automatic access to previous results or automated statistical analysis, both of which are needed to perform delta checks.

Potential errors in POCT report generation also can occur when patient test results are outside the device's validated range.²⁰⁴ Organizations performing POCT must first ensure that the

^v By using QC conducted during routine POCT device use, this institution could avoid having to visually inspect operators regularly and the additional testing and cost involved in routine inspections.

manufacturer's suggested reference interval range applies to their respective patient populations.²³⁶ Lack of QC, operator failure to recognize failures and problems in QC, and the absence or failure of performance-control monitors also can lead to acceptance of invalid results.²⁰⁴ Linking the POCT device to the hospital or laboratory information system allows for age-specific reference ranges, physician alerts, and other warnings to be included with the test results.²⁰⁸

Verification of POCT results can be conducted using computer workstations; in this situation, information flows from the POCT device to the data manager and awaits LIS verification.²³⁷ Expert decision-support functions in the LIS can autoverify the test results using predetermined expert system rules that are consistent with pre-existing rules for results reporting.^{238,239} While few studies have examined autoverification of results received from POCT devices, the benefits of autoverification have been assessed in central laboratory testing. Autoverification of results can speed TAT, improve laboratory workflow, and ease the effect of shortages in laboratory personnel; however, the autoverification process is not error-proof.^{240,241} In order to prevent autoverification of potentially invalid results, the LIS must be able to capture all error flags generated by an instrument. While it raises other concerns, it is likely that autoverification of test results received via POCT offers similar benefits.

Few studies have examined error during autoverification of results received via POCT devices. In a study reported in 2005, a core laboratory located in a large health system analyzed data to improve the rate of amended test results (i.e., correction of reported values after results verification). Investigators reported that 34% of defects identified resulted from autoverification errors made by the LIS.²⁴² However, in a study reported in 2005, a large clinical chemistry and urinalysis laboratory found that the number of inappropriately verified test results decreased following implementation of results autoverification. In instances where results were inappropriately autoverified or prevented from being autoverified, modification of exclusionary setup rules eliminated the problem.²⁴¹

POSTANALYTIC PHASE

Results Interpretation

Incorrect interpretation of POCT results is a source of error that can severely affect the quality of patient care. The potential for results misinterpretation emphasizes the importance of training in all phases of the testing process, including POCT results interpretation.²⁰⁵ It is vital for POCT operators to be aware of the strengths, weaknesses, and limitations of POCT devices, particularly where false positive results may arise from cross-reactivity with foods, medications, and/or metabolites present in the specimen being tested.^{243,244} The NACB's laboratory medicine practice guidelines recommend that organizations agree on and implement procedures that allow only those individuals recognized as being competent to interpret POCT results to do so.²⁴⁵

Relatively few peer-reviewed scientific studies have examined the incidence of POCT errors that are related to results misinterpretation. One study, reported in 2001, used simulated patient case examples with results of blood glucose and urine dipsticks to assess the interpretive abilities of 250 nurses who routinely conduct point-of-care glucose testing. When the results simulated a hypoglycemic patient, 84.1% of nurses correctly interpreted the results; 95.7% of nurses correctly interpreted results simulating a patient with diabetes mellitus. However, only 5.4% of nurses

correctly interpreted the POCT results of a simulation of a case in which the puncture site had become contaminated, falsely raising the capillary blood glucose measurement that, if gone unnoticed, could have led to inappropriate dosage of insulin and other potential consequences.^{205, 246} While this study reported no difference in test interpretation ability according to nurse seniority, others have reported differences in interpretation of POCT results when experienced laboratory personnel read the results versus when non-laboratory personnel perform the interpretation.²⁴⁷

As noted above, linkages between the POCT device and hospital and laboratory information systems also have the potential to diminish errors in POCT results interpretation. Particularly in critical care settings, a POCT operator who has access to the patient's EHR and real-time knowledge of the patient's treatment regimen and other critical physiologic measurements (e.g., pH, PO₂, and hematocrit levels) is more likely to avoid the adverse effects of drugs and confounding variables on POCT device results.^{248, 249}

Critical Value Reporting

The importance of timely and accurate critical value reporting for quality of care and medical error prevention is receiving national recognition.^{250, 251} Reporting of critical values received via POCT presents several opportunities for error. Among these, criticality of the results may not be immediately recognized, criticality may not be noticed by the effective or designated clinical decision maker; and critical results may not be documented sufficiently for subsequent retrieval.²⁰⁴ These errors also can occur during reporting of non-critical POCT results.

In the national survey and consensus process noted above, a group of experts in POCT programs in critical care and other hospital disciplines generated recommendations regarding critical, panic, and alert value reporting and documentation in POCT situations.²¹⁷ Specifically, a list of relevant critical limits should be built into POCT devices and critical results should be stored in an easily accessible manner and annotated. The individual obtaining or the clinician receiving the critical results should be recorded, and verification of critical test results should be requested.

Improved techniques for critical values reporting have arisen from practical experience. As described in a 2007 report, one emergency department at a tertiary care referral center with an annual volume of more than 50,000 patients found that, after implementing arterial blood gas testing at the point of care, critical values were not appropriately reported to physicians in 10 of the first 664 samples run (1.5%).²⁵² After adding a physician "pick list" as a mandatory field, this problem was eliminated for future samples. Emphasis on establishing and improving linkages between the POCT device and the laboratory computer system has played a major role in ensuring that critical values derived from POCT are reported and marked appropriately. A detailed discussion of connectivity can be found in the chapter on Laboratory Information Systems.

Report Formatting

Several types of error can occur during report formatting. Reports that lack units of measurement or use inappropriate units of measurement can lead to harmful misinterpretation of results, particularly when POCT is being used in critical care situations.²⁰⁴ Some POCT devices are not connected to printers, and results are displayed on the device itself; in these cases, results can be misperceived due to their appearance on a small screen.²⁵³ For printed results, POCT device outputs that are unclear also are associated with errors.²⁰⁴

Report Management

The error potential in the final postanalytic step, report management, has not been as widely researched as results reporting. Errors that can occur during report management may result from failure to check initially generated results against subsequently recorded results, leaving users unaware of discrepancies between a POCT device's test result and the patient record; failure to record how clinical users acted upon POCT device results; and delayed recording of results, thereby delaying clinical users' awareness of potentially critical information.²⁰⁴

CONCLUSIONS

The TTP defines the preanalytic, analytic, and postanalytic phases of the laboratory testing cycle, providing a systems-based framework for examining all possible interactions and activities that can affect the quality of laboratory tests. This framework serves as the basis for designing and implementing interventions, restrictions, or limits that can reduce or remove the likelihood of errors that adversely affect testing and patient outcomes.

- Quality activities in laboratory medicine have historically focused on the analytic phase of testing; however, available evidence demonstrates that a higher percentage of errors occur in the pre- and postanalytic phases of testing. The distribution of errors varies widely among institutions and settings. A review of several key studies found error rates of 32-75% in the preanalytic phase, 13-32% in the analytic phase, and 9-31% in the postanalytic phase.
- Poor communication between laboratorians and clinicians during test selection/ordering and interpretation of laboratory findings is an important issue affecting the quality of laboratory services. Although one out of four primary care physicians perceives that the scope of care expected of them is beyond their current knowledge base, they reportedly seek additional information when ordering tests only 30-50% of the time. Medical and scientific advances, such as in genetic testing, will compound challenges associated with ordering the optimal sequence of tests, correctly interpreting results, and incorporating this information into clinical practice.
- While consultations for anatomic pathology are standard practice and reimbursed, this is not always the case in clinical pathology. Yet, when provided, clinical pathology interpretive consultations are well received by physicians. As reported in one study described in this chapter, 98% of physicians found this information to be useful, 59% perceived reduced time to diagnosis, 72% perceived that it reduced the number of tests needed for diagnosis, and 72% believed consults helped to avoid misdiagnosis.
- The most common errors and reasons for specimen rejection during the preanalytic phase are associated with patient and/or specimen misidentification and specimen collection (e.g., insufficient volume, incorrect type of specimen, unusable specimen). Other errors include missing or incorrect information on laboratory test order forms. Among the strategies that are in place or evolving to reduce preanalytic errors are use of barcoded labels for containers and slides, inpatient wristbands with accurate identifying information, and CPOE.

- Analytic errors in clinical pathology typically relate to transcription errors; failure to reject an inadequate or damaged specimen; or bias often caused by interference, instrument calibration error, lot variations, or lack of uniform test values across manufacturers. Automated analyzers and results verification has decreased error rates in clinical pathology substantially over the past decades. Errors that occur in the analytic phase are often the result of errors that originated during preanalytic processes.
- In anatomic pathology, errors may occur during accessioning, in the gross room, or at the microscope, and are classified as specimen/patient identification-related, cognitive-related (e.g., inaccurate conclusions, poor descriptions, knowledge deficits), or cross-contamination-related. External, secondary consultation is common in anatomic pathology; as summarized in one study, original diagnosis was confirmed in 70% of consultations, but significant information was added in 16%.
- Core postanalytic challenges include improving TAT and notification of critical values. Both are key quality measures of the testing process, but are frequently cited for ratings of below-average to poor in customer satisfaction surveys. In clinical pathology, TAT varies by setting, and delays are attributed to staff shortages in preanalytic and analytic phases. In anatomic pathology, TAT varies by specimen type, with delays resulting from difficulty in reaching the clinician for additional information.
- Better integration of laboratory automation and LIS could enable laboratories to identify and diminish error rates in the TTP. This will require much improved communication within and among health care institutions, including, but not limited to systematic provisions for appropriate, timely communication between laboratorians and clinicians.
- Inappropriate test use—including overuse and underuse—can compromise case management, result in adverse health outcomes, and increase health care costs. It arises in tests for screening, diagnosis, and monitoring, and pertains to multiple types of cancer, cardiovascular disease, diabetes, and other prevalent conditions with high clinical and economic burdens and whose course can be affected by proper testing. Sentinel studies in recent years continue to identify and call public attention to inappropriate testing and its contribution to national shortfalls in quality of care. Principles of appropriateness in laboratory medicine are embodied in selecting the right test at the right time for the right patient. Multiple factors lead to inappropriate test use, including test panels that contain unnecessary tests, poorly designed ordering forms, delays in performing tests, failure to use earlier test results, financial incentives, and malpractice concerns. While evidence-based practice guidelines are helping to reduce inappropriate use, continued progress will require greater attention to how elements across the TTP mediate test appropriateness.

Gaps, Needs, and Challenges:

- The day-to-day demands of clinical practice leave physicians with little time to acquire knowledge of new laboratory tests. Furthermore, the average medical student receives 10 weeks or 70 hours of didactic coursework in medical genetics.
- While CPOE has been shown to reduce the frequency of medication order errors, no research has examined the effect of CPOE on correctness of laboratory test orders. As CPOE becomes more prevalent, this effect will need to be better understood.

- Thirty eight states currently allow individuals to directly request that certain laboratory tests be performed on their own blood or urine samples (some in limited capacity) and its popularity is increasing; however, little data exists on the frequency, appropriateness, and quality related to such orders.
- Lack of uniformity and standardization of clinical pathology test values among manufacturers hinders implementation of laboratory-based guidelines, which require method-dependent decision limits. Heterogeneity of test values also makes it difficult for clinicians to work in an integrated health system using more than one testing method.
- The primary barriers to interpretive consultations in clinical pathology reports are lack of reimbursement for such consults and the shortage of true experts with high subspecialty expertise in coagulation, autoimmunity, and other complex areas.
- QC, performance evaluation, and test reproducibility standards to minimize diagnostic discrepancies and errors have been better defined and applied in clinical pathology than in anatomic pathology. Efforts should be undertaken to develop such measures for anatomic pathology.
- The growth of innovative laboratory testing techniques is prompting changes to laboratory report formats. Laboratory reports will need to make better use of graphical displays to facilitate rapid assimilation and comprehension of important data by clinicians, other laboratory professionals, and patients. Standardization of data elements and report formats for laboratory tests is necessary to improve physician comprehension and use of results as well as integrate report data into clinical practice IT applications.
- While the immediate availability of POCT results has the potential to significantly enhance the quality of care, additional research is needed to identify the best methods for integrating POCT into daily clinical processes. Operators of POCT devices must be appropriately trained in testing practices, particularly QC. In addition, methods to improve the accuracy of POCT results relative to those produced in the central laboratory warrants research.

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CHAPTER V

QUALITY SYSTEMS AND PERFORMANCE MEASUREMENT

Quality generally refers to the level of performance or other attributes of interest that are achieved by a product or service. The performance of a product or service can be defined and assessed quantitatively or qualitatively against designated standards or goals, whether for conformance to certain technical standards or specifications or realizing customer satisfaction. Quality improvement programs and systems-based approaches to quality management can contribute to achieving and sustaining high levels of quality.

As described by the IOM, quality in health care is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.¹ High-quality health care is: safe, effective, timely, patient-centered, efficient, and equitable.²

Laboratory medicine contributes significantly to quality of care when tests and related services are clinically appropriate and provided in a technically competent manner with good communication. This chapter provides an overview of the status of systematic approaches to quality and performance measurement in laboratory medicine.

APPROACHES TO QUALITY SYSTEMS IN LABORATORY MEDICINE

Public and private sector organizations in health care, including those associated with laboratory medicine, have described the need for patient care that consistently provides the highest levels of quality and safety. Serious adverse events resulting in patient harm or death have prompted consumer and provider demands for greater quality and led to many of today's quality improvement initiatives. Even so, most initiatives to address quality and safety issues are undertaken with limited resources.^{2,3}

Quality assessment in laboratory medicine has evolved from narrowly focused activities of QC to more comprehensive, systematic methods. For over 50 years, laboratories have instituted diverse, evolving mechanisms to improve the quality of testing. Until 1967, efforts generally targeted improvement in testing accuracy and precision for common analytes through the use of PT. This is an external quality assessment process that evaluates and grades the laboratories' analytic performance of selected tests. Unfavorable performance rates decreased somewhat with use of PT as the sole means of measurement. Passage of the Clinical Laboratory Improvement Act of 1967, corresponding Amendments of 1988 (CLIA), and 1992 implementation of the final CLIA regulations standardized the approach to laboratory quality. The regulations established minimal standards for QC; QA practices; PT; personnel qualifications and responsibilities; patient test management; and recordkeeping. The specific requirements that laboratories must meet are based on the complexity of the testing performed.⁴ Laboratories performing moderate and high complexity testing, including hospitals, reference laboratories, and POLs, meet these standards in order to be certified.^a Laboratories performing relatively simple tests categorized as "waived" are

^a Refer to the chapter on Federal Regulatory Oversight and Appendix A of this report for additional information about CLIA regulations.

not subject to CLIA standards, but are required to follow manufacturers' instructions for test performance and QC.^b (Definitions of QC and QA are provided in Box 5.1 below.)

QC and PT activities are reported to have had key roles in the reduction of errors associated with the analytic phase of testing.^{5,6} According to the American Proficiency Institute, PT failure rates^c for chemistry and hematology laboratory tests decreased from 1994 to 2004 for eight analytes most often tested in physicians' office and clinical laboratories.⁷ PT failure rates decreased from 18.7% to 3.2% for cholesterol, from 6.3% to 1.1% for potassium, and from 5.7% to 2.4% for creatinine. Failure rates for testing microbiology analytes decreased for both positive and negative cultures between 1994 and 2004. Another study demonstrated decreases in deficiencies associated with inspections. During 1995-1996, 30% of laboratories inspected to assess compliance with CLIA failed to perform QC testing and 13% failed to follow directions outlined by manufacturers. By 2001-2002, 18% of CLIA inspected sites failed to perform QC testing and 6% were not following manufacturers' directions.⁸

While performance in the analytic phase of testing as evaluated by basic QC, QA, and PT has improved substantially since CLIA's implementation, further improvements are necessary to achieve quality and safety. The findings of CMS oversight activities, academic studies, and accrediting organization surveys reinforce the need to move beyond analytic-focused activities to a mechanism that supports integration of preanalytic, analytic, and postanalytic components as described in the chapter on the TTP in this report. Such concerns arise, for example, when inadequate specimen volumes are obtained during collection, affecting the laboratory's ability to test the specimen in the analytic phase. Improvements in quality and safety at each critical control point along the path of the TTP require the extensive framework and methodologies inherent in systems-based approaches to quality management. A critical control point is a point, step, or procedure at which control can be exercised to prevent, eliminate, or minimize a hazard.⁹

The introduction of comprehensive systems-based approaches has been of interest to public and private sector stakeholders associated with laboratory medicine. Several laboratory accrediting organizations took the lead in promoting the adoption of systems approaches voluntarily or as a condition of accreditation during the 1990s and early 2000s. The Joint Commission, CAP, AABB (formerly the American Association of Blood Banks), COLA, and American Society for Histocompatibility and Immunogenetics (ASHI) advocate the implementation of comprehensive quality management systems (QMS), beyond the basic requirements of CLIA.¹⁰⁻¹³

In 2003, CMS restructured the QC and QA provisions in CLIA to reflect the flow of specimens through the laboratory, and integrated QA into all phases of testing. The requirements now correspond to the broader framework of formalized systems-based approaches to quality management.

^b Some states (e.g., New York, Washington) have more stringent requirements.

^c Failure rate is defined as: (number of unacceptable responses/ total number of responses) x 100.

Beyond the Basics to Quality Management Systems

The Clinical and Laboratory Standards Institute (CLSI)^d adopted a hierarchical model defining five tiers of quality.¹⁵⁻¹⁷ As presented in Box 5.1, QC and QA are precursor, lower-tier activities. Mid-level tiers include the introduction of quality management systems and quality cost management. Long-term success in all tiers is necessary to maintain the highest levels of excellence and total quality management (TQM), generally known as continuous quality improvement (CQI) in health care.

Most health care organizations are operating at or below the level of QA, although some organizations, such as the Veterans Health Administration (VHA) and Latter-day Saints hospital (Salt Lake City), are working successfully with strategic tools to implement quality management systems (e.g., CQI, failure mode and effects analysis [FMEA]).^{18, 19} Efforts over the last decade to redesign health care delivery systems have promoted adoption of the two higher-level activities: QMS as a tool for quality, safety, and performance measurement; and pay-for-performance programs, which, though largely unproven to date, may contribute to quality cost management.

QMS have been used in a wide variety of applications to achieve major improvements in the quality, efficacy, safety, and/or customer-centeredness of processes, products, and services in a full range of manufacturing and service industries.²⁰ QMS incorporates principles of engineering, manufacturing, and human factors science to establish an integrated infrastructure that optimizes and continually improves health care operations. Structures, processes, and/or events are considered together as they interact to produce an outcome.²¹ Whether or not system components cross departmental or organizational boundaries, a single change anywhere in the system can affect other parts of the system. The systems approach supports workflow design; performance monitoring; management of organizational, personnel, and informational factors; and leveraging technology and other contributing factors for a well-defined, constantly evolving, coordinated mechanism to produce desired outcomes and continuously improve quality.

Organizations that implement the QMS model can greatly enhance their ability to reduce or eliminate errors, meet customer needs, perform well on accreditation assessments, and maintain quality objectives.²² However, the broader health care sector largely has been slower to adopt QMS, even though the small but growing number of health care organizations that have applied them are reporting favorable returns.²³⁻²⁵

^d CLSI is a non-profit standards-developing organization that promotes the development and use of guidelines and standards within the health care community, including clinical laboratories.¹⁴

Box 5.1: Five Levels of Quality—Definitions

Level 1: Total quality management is intended to sustain high quality by focusing on long-term success through customer satisfaction. TQM holds quality as the driving factor behind leadership, design, planning, and improvement. Variations from quality are artifacts of poorly designed systems, rather than the fault of one or more individuals.^{19, 26}

Level 2: Quality cost management (QCM) includes all activities involved in QMS, QA, and QC, along with related economic aspects (i.e., “cost of quality”).²⁷ QCM promotes integration of quality processes throughout an organization subject to the constraints of the organization’s financial resources.²⁸ Budgeting and resource allocation are integrated within the context of the larger organization and oriented to meeting physician and patient needs. Recent efforts to implement pay-for-performance programs may be considered a form of QCM.

Level 3: Quality management systems refers to a systematic approach to achieving quality objectives.¹⁸ QMS constitutes a coordinated and comprehensive effort to meet quality objectives using management systems standards such as those developed by the International Organization for Standardization (ISO) and CLSI.²⁸ Standards for QMS are implemented in laboratory medicine via such models as CQI, Six Sigma, failure mode and effects analysis, and Toyota “lean production.”

Level 4: Quality assurance/assessment monitors the totality of components or characteristics that affect quality and customer satisfaction.²⁹ QA involves planned and systematic activities to provide confidence that an organization fulfills requirements for quality. Regulatory and compliance issues are generally handled through QA-related policies and procedures. In laboratory medicine, characteristics such as turnaround time, patient preparation, and specimen collection may be monitored at a basic level internally and externally. Proficiency testing is an external mechanism for QA.

Level 5: Quality control refers to laboratories’ internal procedures for day-to-day monitoring of instruments, monitoring work processes, detecting problems, and making corrections prior to the delivery of products or services.²⁹ Typically, QC procedures for monitoring analytic performance rely on statistical measures (e.g., mean performance and within ± 2 standard deviations) as an indicator of quality.²⁸ For example, the precision of clinical laboratory tests performed for a specific analyte is assessed relative to its reference standard. QC is a targeted, internal mechanism.

Source: A quality management system model for health care. Approved guideline: HS1-A2; second edition. Wayne, PA: Clinical and Laboratory Standards Institute, 2004.

Standards and Guidelines for Quality Management Systems

Formalized standards and guidelines for QMS that encompass these properties have been developed by the International Organization for Standardization (ISO)^e as well as other institutions involved in a specific sector such as CLSI for health care and laboratory medicine. In many instances, accreditation organizations use the standards as a framework for developing detailed criteria and benchmarks appropriate to the respective medical discipline or subspecialty.

Standards can serve several purposes. They can establish consistency or uniformity across multiple individuals and organizations, and set expectations of quality and safety for organizations, health professionals, patients/consumers, and purchasers. Because the standards for QMS are based on the day-to-day activities of health care professionals, they are an effective means for improving care delivery.²¹ Measurement of performance against designated standards and feedback about that performance are important parts of QMS-related quality improvement initiatives.

^e ISO develops international standards that outline the requirements for products, services, processes, materials, and systems and are designed to be implemented by organizations worldwide.³⁰ The American National Standards Institute is responsible for endorsing consensus standards in the U.S. and for representing U.S. interests at the ISO.

ISO and CLSI standards for QMS are internationally recognized. The ISO 9000 series^f is considered the world standard for establishing, verifying, and certifying QMS. It was developed to assist diverse organizations with implementation and operation of effective QMS, regardless of the service or product provided.^{32, 33} Aside from manufacturing-related industries such as medical devices and pharmaceuticals and select high-risk specialty areas, ISO 9001:2000 has not been implemented on a widespread scale in the U.S. health care sector. As of 2005, about 100 health care entities in North America were certified to ISO 9001:2000, including 12 hospitals and 10 medical groups in the U.S.³⁴ ISO 9001:2000 has been more widely adopted by international health care facilities. A 2006 survey estimated that 14,180 certificates for ISO 9001:2000 have been issued worldwide in the health care and social work sectors.³⁵

Historically, the standards have been employed in other sectors; about 90% of facilities in the U.S. certified to the ISO 9001:2000 standard are involved in manufacturing.³⁴ However, public and private sector stakeholders are interested in shifting the largely fragmented U.S. health care system that produces inconsistent levels of quality to more integrated, dynamic system capable of producing and sustaining high levels of quality. Their efforts have prompted renewed interest in the use of standardized QMS, including ISO 9001:2000, to facilitate this transformation.²⁰ Certain U.S. government agencies, including CMS, are requiring certain health sector contractors be certified to ISO 9001:2000 or undergo a third-party validation process.³⁶

Because of the broadly applicable nature of ISO 9001:2000, more targeted standards for QMS have been developed for health care, often according to specialty area. CLSI is the chief developer of standards for laboratory medicine and serves as the Secretariat^g for the ISO Technical Committee on Clinical Laboratory Testing (ISO/TC 212). Through the ISO/TC 212 workgroup on quality management, CLSI led the development of ISO 15189 – *Medical Laboratories – Particular Requirements for Quality and Competence*, a standard for process-based QMS specifically in clinical laboratories. ISO 15189 addresses all aspects of laboratory operation, from patient preparation and identification to the collection and examination of clinical samples, as well as document control, contracts, and relationships with referral laboratories.³⁷ Other standards target specific uses or elements of QMS.^h Since the approval of ISO 15189, CLSI has sold at least 280 copiesⁱ of the standard to laboratories in the U.S.³⁸ Beyond this expression of interest, it remains to be seen how many of these laboratories will implement the standard.

As a complement to the ISO standards, CLSI developed two guidelines that advance the implementation of QMS. The first, GP26-A3 - *Application of a Quality Management System Model for Laboratory Services*, defines the laboratory path of workflow and provides direction on the design of policies, processes, and procedures to build required levels of quality into day-to-day operations and reduce the potential for errors and wasted resources.³⁹ The second guideline, HS1-A2 - *A Quality Management System Model for Health Care*, supports ISO 9001:2000 and 15189 and describes

^f ISO 9000 was established in 1987. Its precursor was BS 5750, developed during the 1960s and 1970s by the British Government.³¹

^g As Secretariat for ISO/TC 212, CLSI coordinates international standardization of clinical laboratory testing in four areas: quality management in the clinical laboratory; reference systems; IVD products; and antimicrobial susceptibility testing.

^h Other standards related to QMS include: ISO 15190 – *Medical laboratories – Requirements for safety*; ISO 22869 - *Clinical laboratory testing – Guidance on application of ISO 15189*; ISO 22870 - *Point-of-care testing – Requirements for quality and competence*; and ISO 22367 - *Medical laboratories - Reduction of error through risk management and continual improvement*.

ⁱ This figure does not account for copies of the ISO 15189 standard sold by ANSI, which was unavailable.

the set of 12 essential components that must be in place for an organization to function in a manner that meets QMS standards and quality objectives (see Box 5.2).¹⁸ These components, known as quality system essentials (QSEs), provide guidelines to describe, document, integrate, measure, and monitor the implementation and effectiveness of the work operations of any organization, service unit, or support function in the organization. Subsequent editions of GP26-A3 also incorporated laboratory-specific guidelines for implementing essential components of QMS identified in HS1-A2.^j The 12 QSEs are applied to every step in the path of workflow (e.g., test ordering, specimen collection) to ensure that all quality management issues are identified and addressed in the organization's policies and procedures.

Box 5.2: Quality System Essentials

- Documents and records
- Organization
- Personnel
- Equipment
- Purchasing and inventory
- Process control
- Information management
- Occurrence management
- Assessment: external and internal
- Process improvement
- Customer service
- Facilities and safety

Source: A quality management system model for health care. Approved guideline: HS1-A2; second edition. Wayne, PA: Clinical and Laboratory Standards Institute, 2004.

Standards for QMS have been most broadly adopted in transfusion medicine. Beginning in 1990, the AABB recognized the need for QMS specifically applicable to blood banking in order to move from an error-detection approach to an error prevention approach.⁴⁰ Initially, the AABB Quality Program was designed to meet FDA requirements for Current Good Manufacturing Practices and QA guidelines. To enhance user friendliness and encourage greater acceptance, AABB revised the program in the late 1990s by relying on ISO 9001:2000 standards to develop a specific set of QSEs for blood banking. In 1998, AABB began requiring full implementation of quality systems for accreditation.⁴¹

Use of ISO 9000, ISO 15189, and CLSI GP26-A3 in laboratory medicine has accelerated in recent years as CMS and other laboratory accreditation organizations incorporate QMS-related standards and guidelines into their regulatory requirements.^{42, 43} In 2003, CMS used the path of workflow as the model for restructuring the CLIA requirements. CMS also has mapped the revised CLIA provisions to the QSEs outlined in CLSI GP26-A3 to demonstrate that laboratories interested in using the QSEs can achieve CLIA compliance concurrently.

^j Other CLSI documents supply discipline-specific details (e.g., QC for quantitative measurements, reference intervals) as a compliment to HS1-A2 and GP26-A3.

Also in 2003, CAP endorsed ISO 15189 accreditation as a value-added program,^k with optional use of CLSI QSEs as a supplement.⁴⁴ CAP's Laboratory Accreditation Program General Checklist requires that laboratories have a documented quality management program that can be based on ISO 9000, ISO 15189, or programs designed by CAP, other organizations, or laboratories themselves.⁴⁵ At this writing, at least three laboratories are seeking accreditation to ISO 15189 through CAP.⁴⁶ Similarly, COLA announced the launch of new interactive QMS training courses based on ISO 15189 and CLSI guidelines in 2005.⁴⁷ COLA supports implementation of QMS voluntarily; its standards for laboratory self assessment do not require QMS as a condition for accreditation.

Among the main potential benefits of U.S. harmonization to ISO standards are:

- Laboratories can implement proven quality improvement strategies without additional regulation
- Accreditation organizations can maximize their ability to evaluate laboratories worldwide
- Vendors can standardize instruments more easily
- Researchers can undertake cross-laboratory and cross-national comparisons of performance^{48, 49}

The following section provides a brief summary of available research on specific QMS-related tools.

Implementing Quality Management Systems

The strategic tools for implementing systems-based approaches to quality management and improvement in health care and laboratory medicine include methods such as CQI, Toyota "lean production," Six Sigma, and FMEA. These methods have been validated as effective quality management tools in various sectors in the U.S. and worldwide, such as the automobile industry, telecommunications, mining, banking, and construction.²⁰ Although use of these methods is not widespread in laboratories at this time, an increasing number of laboratories, from small POLs to large reference laboratories, are employing them to meet and exceed regulatory and accreditation requirements as well as clinician and patient expectations for quality and financial management objectives.

Among the most commonly used QMS tools, CQI, lean production, Six Sigma, and FMEA share several key features:

- Scientific approach to process analysis and systems improvement
- Decision-making based on data derived from regular performance measurement
- Improvement focus
- Preventive orientation toward potential quality problems and errors
- Interdisciplinary teams⁹

^k CAP's program supporting ISO 15189 is separate from its CLIA accreditation program.

Continuous Quality Improvement

CQI applies the scientific methods of TQM¹ to process improvement in health care and may be employed to improve clinical quality, patient satisfaction, error rates, waste, unit production costs, productivity, and market share, among other aspects of care.¹⁹ It embodies a disciplined approach to managing competitive challenges and enhancing customer satisfaction. CQI is intended to reduce variation and improve performance through a four-step cycle: The teams *plan* an intervention to improve the process; *do* the hypothesized intervention; *study* the results of the intervention; and *act* on the results. Cross-cutting teams devise a flow chart of a work process to be studied and use data to understand variations in performance.⁹

The CQI movement began in academic research institutions during the mid-1980s and gained momentum when The Joint Commission adopted the philosophy to advance health care quality improvement goals.⁵⁰ The movement is helping to promote dynamic quality management, establishing the patient as the true “consumer” of health care services, and motivating health care organizations to initiate quality improvement programs. Although some health care leaders have claimed successful use of CQI to achieve quality goals, few studies are documented in the literature. For example, a regional group of cardiothoracic surgeons that implemented a CQI intervention reported reduced mortality associated with coronary bypass surgery by 24%.⁵¹ A Veterans Administration medical center used CQI to increase operating room efficiency, noting procedure start time improvements ranging from 30 to 55 minutes.⁵² In a randomized controlled trial, patients assigned to protocol-directed weaning from ventilation tubes as developed via CQI methodology had significantly shorter durations of mechanical ventilation compared with patients assigned to physician-directed weaning.⁵³

Laboratories have demonstrated some successes with CQI. Implementing CQI for physicians’ ordering of blood for surgical cases at a regional hospital facilitated savings of more than 500 hours of technologist time and \$350,000 in patient charges over a two-month period. Reduced inventory and blood banking costs added further to cost savings.⁵⁴ A dedicated stat laboratory implemented CQI to improve TAT for various clinical pathology tests, after which TAT decreased from 61 to 36 minutes for clinical chemistry tests.⁵⁵ In a two-year study applying CQI to physician ordering of preoperative tests for elective surgery, the volume of tests ordered decreased by 50% and 60% in the first and second years, respectively, the appropriateness of test orders improved by 81% and 86%, and overall cost savings were \$76,000.⁵⁶ CQI also has been applied successfully to POCT, leading to more reliable results and helping resolve discrepancies between test results received at the bedside versus in the core laboratory.^{57, 58}

There are notable challenges to implementing CQI. Lack of hospital or physician administrative and financial support were identified as barriers to CQI implementation by 4 of 9 hospital catheterization laboratories participating in a CQI initiative during 1998-2002.⁵⁹ The extensive time involved in educating staff about CQI principles and forming and working together as teams, along with insufficient commitment to CQI on the part of hospital management were cited as key obstacles to implementation by a hospital-based pathology department.⁶⁰

¹ Originally introduced to Japanese manufacturers in the 1950s, TQM gained popularity in the U.S. in the late 1970s and early 1980s as an alternative to QA.¹⁹

To date, the impact of CQI on the health care sector has not been as widespread as initially expected. This apparent lag in uptake has been attributed to such reasons as:

- The literature documenting quality improvement and clinical outcomes stemming from CQI remains relatively sparse.
- Administrators, rather than clinicians, were the first who sought to incorporate CQI, which may convey to some observers that it is a mechanism for cutting costs rather than improving quality.
- Implementation was not as easy as anticipated, frustrating many of the leaders who initially advocated CQI.¹⁹

While the concept of continuously improving performance to achieve quality remains intact, other methods have emerged for improving quality.

Six Sigma

Developed by the Motorola Company in the early 1980s, the Six Sigma system is a means of improving quality by identifying and taking action at the root cause of a problem, rather than on symptoms arising from the cause.^{28, 61} Six Sigma identifies direct relationships between the number of defects in a given product or process, wasted resources, and the level of customer satisfaction.⁶² Six Sigma is similar to TQM but has been described as having a more aggressive goal. The objective of Six Sigma is to reduce defect rates to low frequencies in a statistical distribution, based on multiple standard deviations from a specified average, such as fewer than 3.4 defects per million opportunities. Table 5.1 displays the Six Sigma performance scale.

Table 5.1: Six Sigma Performance Scale

Process Sigma	Percent Accuracy	Defects per million opportunities
6	99.9997%	3.4
5	99.98%	233
4	99.4%	6,210
3.5	97.7%	22,700
3	93.3%	66,807
2	69.1%	308,537

Source: Westgard JO, Westgard SA. The quality of laboratory testing today: an assessment of sigma metrics for analytic quality using performance data from proficiency testing surveys and the CLIA criteria for acceptable performance. *Am J Clin Pathol* 2006;125(3):343-354.

Six Sigma can be used in laboratory medicine to establish tolerance limits necessary to define good quality. Westgard has described two methods for calculating the sigma metric – one method is based on measuring the outcome of the process, whereas the other method is based on measuring the variation of the process directly.⁶³ The outcome measurement approach involves counting defects, calculating defects per million, and using a statistical table to convert the defect rate per million to a sigma metric. This approach is applicable to any process but usually requires extensive efforts to collect and analyze the data. As such, it is typically applied to preanalytic and postanalytic processes. Direct measurement of process variability (i.e., standard deviation) allows for determination of process capability. It assumes that the process distribution is stable and can be characterized by repetitive measurements. Thus, this methodology is used to determine the

precision and accuracy of analytic processes through experimental procedures. A sigma metric is calculated from the defined tolerance limits and the variation observed.⁶⁴

Studies using both sets of metrics have reported that laboratory testing falls short of the minimal acceptable performance level demanded by other industries. Based on CLIA criteria for acceptable performance in PT, the national quality of cholesterol testing is estimated at 2.9 to 3.0 sigma, glucose at 2.9 to 3.0, calcium at 2.8 to 3.0, and PSA at 1.2 to 1.8.⁶⁴ This level of quality was deemed adequate only if performance was controlled with QC above that required by CLIA. Reported defect rates for other common laboratory measures are approximately 2.8 sigma for Papanicolaou smears, 2.3 sigma for therapeutic drug monitoring, and 3.6 sigma for transport of red blood cells.⁶⁵ Among other factors, these lower levels resulted from missing information in test requests (preanalytic errors) and incorrect laboratory measurement (analytic errors). However, designating a tolerance level such as 3.4 defects per million for all processes is arbitrary; it may be unacceptably high for some critical processes and unnecessarily difficult and costly to achieve for others.

Six Sigma provides clinical laboratories with the methodology and measurements to determine specific QC actions necessary to achieve the desired level of quality.⁶⁴ Also, Six Sigma allows for communication of quality metrics in a format that is understood outside the health sector.⁶¹ Health care institutions and laboratories can compare performance against that of other sectors.

Six Sigma is gaining acceptance in health care and laboratory medicine as a method to generate objective metrics and estimates of quality, though implementation is still in the early stages.⁶⁶ The following examples highlight case studies of organizations that have experienced modest improvements in use of Six Sigma for measuring and improving performance.

In 2004, West Tennessee Healthcare's core lab built its new laboratory using lean production and Six Sigma principles. Focusing on phlebotomy, Six Sigma principles were used to assess the timeliness with which phlebotomists worked and to identify best practices.⁶⁷ As a result, the time required to get phlebotomy specimens to the laboratory decreased from over 20 minutes to an average of 5.2 minutes. Not one patient identification error was detected and documented during the subsequent 11 months.

In another study using a combination of lean production (described in the next section) and Six Sigma, Washington Hospital Center's Automated Services Laboratory (Washington, DC) identified 6 changes that could improve laboratory quality and turnaround time, including decreasing centrifuge times and taking steps to eliminate blood clotting.⁶⁸ The laboratory reduced mean TAT for blood tests from 75 to 46 minutes and decreased its annual operating cost by nearly \$80,000.

North Shore-Long Island Jewish Health System (Great Neck, NY), which includes a network of laboratories that together process 3.5 million examinations annually, used Six Sigma to reduce the number of accessioning errors, or errors occurring when patient data is entered, tests are ordered, or samples are labeled.⁶⁹ Six Sigma methods helped staff to identify specific steps in the accession process that were most often completed incorrectly or incompletely. Following implementation of barcoded labels and a new training program for accessioners, the performance of the accession department improved from 3.9 sigma to 4.5 sigma.

Toyota (Lean) Production System

Lean production, also known as the Toyota Production System, was developed and perfected by the Toyota Automotive Company over the latter half of the twentieth century. It is based on the tenet that consistently eliminating waste in each step of a process leads to increased efficiency (i.e., the best quality and lowest cost), while improving safety and morale.^{70,71} Lean production aims to meet internal and external customer needs through a one-by-one continuous flow process with integrated quality indicators and elimination of system waste related to materials, time, idle equipment, and inventory. The system design highlights problems in real-time where the work is performed and is intended to solve problems at their root cause. Front-line workers are empowered to participate in decision-making, design changes, and problem-solving at the time errors occur. The overarching goal is to reduce all system defects to zero.

Studies of lean production in laboratory medicine have reported successful results. One study sought to improve chemistry test turnaround time in a central laboratory by addressing preanalytic variables using existing resources and lean production. The redesigned preanalytic process had fewer steps and employed the one-piece flow system^m to move specimens through the accessioning, centrifugation, and aliquoting process. Five new workstations were added and others redesigned for efficiency. Median preanalytic processing time was reduced from 29 to 19 minutes and the laboratory met the goal of reporting 80% of chemistry results in less than 1 hour for 11 consecutive months. Introduction of lean production also eliminated systemic waste, including reduction in mislabeled and missing tubes, and elimination of the unwritten and unapproved practice of collecting an extra tube of blood, which decreased the number of tubes used for collection, number of tubes processed per month, and amount of biohazardous waste discarded.⁷²

One study examined implementation of lean production in a single clinician's office practice and cytology laboratory to determine its impact on Pap test quality and errors.⁷³ The clinician's goal was to obtain a perfect specimen for every patient, i.e., one that adequately sampled the transformation zone in which preneoplastic lesions usually develop. Test quality improved, as the percentage of Pap tests without a transformation zoneⁿ component decreased from 9.9% to 4.7%; the percentage of tests with a diagnosis of atypical squamous cells of undetermined significance decreased from 7.8% to 3.9%; and the frequency of error as measured by cytologic-histologic correlation decreased from 9.52% to 7.84%.

Use of lean production in process redesign was used to diminish diagnostic errors associated with examination of thyroid gland fine-needle aspirations by cytologists and cytotechnologists at two different hospitals.⁷⁴ This procedure was chosen due to the wide variability in diagnostic accuracy indicated in the literature.⁷⁵⁻⁷⁷ For the study, the investigators created a specimen adequacy scoring system, used standardized diagnostic terminology, and incorporated an immediate interpretation service. Performance changes following the use of standardized terminology included (but were not limited to) an increase in test sensitivity from 70.2% to 90.6%, decrease in the false-negative rate from 41.8% to 19.1%, decrease in the discrepancy rate from 31.0% to 24.2%, and increase in the uninterpretable specimen rate from 5.8% to 19.8%. With the

^m In a one-piece flow system, all activities involved in a process are performed on each object before work is begun on the next object.

ⁿ On the cervix, there are two cell types, squamous cells and columnar cells, which meet at a place called the squamo-columnar junction, also known as the transformation zone. It is in this transformation zone that abnormal growth or dysplasia develops.

addition of the immediate interpretation service, the noninterpretable specimen rate decreased significantly from 23.8% to 7.8%.

As with any QMS tool, the success of lean production depends on the commitment of the organizational leadership and staff in adopting the methodology and managing expectations for realizing practical gains.⁷⁸

Failure Mode and Effects Analysis

Though it is not considered to be a comprehensive approach to quality management, FMEA is a tool that supplements and contributes to QMS by providing a mechanism to systematically evaluate and prevent errors (“failures”) that can cause harm. FMEA is a team-based, proactive approach for identifying the ways that a process or design can fail, why it might fail, and how it can be made safer.⁷⁹ Although originally developed and used by the U.S. military and space program, the VHA and Tenet Health System have adapted the approach for identifying and preventing medical errors and other process-related problems.¹⁹ In 2001, the VHA’s National Center for Patient Safety introduced Health Care Failure Mode and Effect Analysis™.⁸⁰ That same year, The Joint Commission established a new standard that requires all accredited hospitals to proactively assess at least one high-risk process per year, such as the preparation of medication or plans for infection control, using such methodologies as FMEA.^{10,81} When sentinel events occur, organizations must undertake not only the traditional retrospective root cause analysis, but the prospective FMEA as well. The requirements were extended to home care programs in 2004.⁸² Typically, organizations initiate an analysis when a near miss or concern for risk occurs rather than only when a sentinel event occurs.⁸³

FMEA facilitates identification, evaluation, and calculation of risk for each failure mode (e.g., problem or defect) according to severity, frequency, and detectability. Each characteristic is assigned a value between 1 (highest) and 10.²⁸ The ultimate “effect” or risk priority number for a particular failure mode is determined by multiplying the scores for each characteristic: Effect = Severity x Frequency x Detectability. Higher risk priority numbers indicate the need to prioritize actions to correct problems.¹⁹ Health care organizations report positive results from use of FMEA in a range of clinical processes such as trauma care, chemotherapy, case management, blood transfusion, and other areas of laboratory medicine.⁸⁴⁻⁸⁷

FMEA has multiple functions in laboratory medicine. First, FMEA can be used in product development. CLSI guideline EP18-P2, *Risk Management Techniques to Identify and Control Laboratory Error Sources*,^o refers to FMEA as a means for manufacturers of POCT devices to evaluate potential failure modes during the design and development of new products as well as to ensure the ability of users to detect and remedy possible causes of error.⁸⁸ Second, FMEA can reduce risk in all phases of the laboratory testing process through evaluation and measurement of hazards associated with process malfunctions, decision making to determine where and how to execute improvement actions, and measurement of outcomes from improvement actions.^{28, 85}

Several laboratories have successfully implemented FMEA. For example, in 2003, the Los Angeles County and University of Southern California Healthcare Network used FMEA to decrease the time in which they reported critical laboratory values to licensed caregivers of

^o EP18-P2 is a revision of a previously developed guideline EP18-A, *Quality Management for Single-Use Testing*.

outpatients and non-critical care inpatients.⁸⁹ Average monthly notification time declined steadily over the 8-month period after system redesign to target areas likely to result in improved outcomes. Another study of a children's hospital network used FMEA to identify the preanalytic specimen labeling phase as the key focus area for improvement.⁹⁰ After laboratories adopted the practice of accepting only those patient specimens that met Joint Commission standards for labeling, the number of mislabeled and/or unlabeled specimens decreased by 75%. In a study of transfusion errors in a hospital setting, laboratorians used FMEA to ascertain vulnerabilities in day-to-day procedures and redesign processes to prevent errors.⁸⁴ The new process accomplished its goal of preventing all serious avoidable errors during the three-month pilot study and in the eight months following laboratory-wide implementation. Although a few measures indicated the need for occasional coaching to reinforce the procedural changes, the number of variances among staff continued to steadily decrease.

Laboratories and other health care organizations can encounter challenges when using FMEA. As noted by the VHA, groups that attempt to implement too many actions, fail to communicate with team members who will actually be responsible for implementing changes, and do not gain backing from senior management often find the FMEA process ineffective.⁸⁰

Considerations for Designing Quality Management Systems

QMS implementation presents specific challenges in different laboratory settings. Hospital and physician office laboratories often cite resistance to cultural change as a major obstacle barring implementation of QMS. A leadership team that is competent, effective, and enthusiastic is vital to successful implementation in POLs and hospital laboratories. In particular, team members should possess substantial knowledge about the processes in need of improvement as well as the QMS methodology being implemented.⁹¹⁻⁹⁴ Commitment to change by other laboratory personnel also is necessary and can be achieved by involving all staff in QMS deployment, data collection and analysis.^{69, 91, 92} Recognition of team members' progress is important to group learning and continued internal support for QMS implementation.⁹²

Some POLs, hospital, and reference laboratories have cited financial constraints and the belief that QMS costs more than it saves as obstacles to its implementation. Strategies to minimize the cost of QMS implementation include thorough review and selection of the QMS methodology that most closely matches the organizational goals and budget and partnership with other health care professionals whose work is significantly related to the laboratory (e.g., clinic administrators, physicians, nurses).^{91, 95} From these strategies, laboratories have reported increasing returns on their investment and additional opportunities for funding of QMS.⁹⁶

Certain observers question the ability of QMS tools (i.e., CQI, lean production, Six Sigma, FMEA) to improve the quality of patient care.⁴⁹ Despite their face validity, the use of QMS tools may not have been studied sufficiently to date, providing limited evidence of their effectiveness. There is considerable variation in QMS applications, which may create challenges to comparisons of one methodology to another. Further study of these tools in accordance with clearly defined standards would help to build an objective evidence base.

PERFORMANCE MEASUREMENT

The development and use of objective measures to evaluate the quality of health care is essential for improving health care delivery.⁹⁷ Information derived from measurement facilitates an understanding of how health services, organizational factors, and financial factors affect patient and population health, and other important effects arising from differences in patient population, health conditions, and settings of care.⁹⁸ This information can support decisions to change resource use and delivery.

Measurement of quality serves key health care objectives, specifically to:

- Inform quality improvement efforts
- Inspect and certify that a facility or provider meets previously established standards
- Compare groups for a variety of purposes, including selective contracting by purchasers and choice of providers and practitioners by individuals
- Support decisions by patients, families, and employees about selecting health care providers and facilities
- Identify substandard performers, particularly those whose performance is so far below an acceptable level that immediate actions are needed
- Highlight, reward, and disseminate best practices
- Monitor and report information about changes in quality over time⁹⁸

The data from measurement allows an organization to assess performance, use that information to improve, and increase the likelihood of achieving desired health outcomes based on current professional knowledge.⁹⁹ Performance measurement has been a core feature of improvement programs for many public and private sector QA organizations in health care for more than 15 years (see Box 5.3 for a brief synopsis). While laboratory testing is incorporated to some extent in most of these organizations' performance measurement programs, the focus tends to be on clinician ordering and patient receipt of appropriate tests for screening, diagnosis, or disease management purposes. These organizations do not directly address measurement and reporting of key components of quality and performance related to the total laboratory testing process. Assessments of this nature, though very limited, are performed by laboratory sector oversight, research, and professional organizations.

The need for a standardized set of measures to report on key aspects of quality across the TTP has been under discussion for the last decade.¹⁰⁰ In the last few years, CDC and other organizations have sponsored studies that may facilitate the development of a national framework and performance measures for laboratory medicine.

Box 5.3: Performance Measurement Initiatives in Health Care

The importance and utility of routine, externally reported assessments of the quality of health care delivered is widely recognized and accepted.¹⁰¹ Efforts to standardize quality measurement and reporting in the health care system have been underway for more than 15 years.¹⁰² Largely driven by federal and private sector payers and accrediting organizations, early leaders in performance measurement include: CMS, AHRQ, The Joint Commission, and NCOA (a coalition of private sector health plans). NCOA's Health Plan Employer Data and Information Set (HEDIS)^P is one of the most successful quality measurement initiatives to date. Initially, health plans seeking accreditation by NCOA were required to report on HEDIS measures. However, when the measures were adapted in the mid-1990s for use by public purchasers, CMS began to require plans participating in Medicare programs to report on the measures as well.¹⁰³ Today, the measures also are used by private purchasers in nearly 90 pay-for-performance programs.¹⁰⁴

Other organizations have joined efforts to develop, coordinate, and harmonize performance measurement and reporting. These include the Pacific Business Group on Health, the Leapfrog Group, American Medical Association, Hospital Quality Alliance, Ambulatory Care Quality Alliance, the Foundation for Accountability, and National Quality Forum (NQF). Standards and requirements for quality assessment, performance measurement, and public reporting have extended to long-term and ambulatory care settings. Performance measures also are becoming more specific for patient populations (e.g., children, elderly), health conditions (e.g., substance abuse disorders, venous thromboembolism), and infrastructure (e.g., health information technology).¹⁰⁵

Basics of Performance Measurement*Types of Performance Measures*

Generally, performance measures are classified into three broad categories based on Donabedian's classic paradigm for evaluating quality of care.¹ Each dimension has a direct influence on the next.

- **Structural** measures are used to evaluate the organizational (e.g., policies and procedures), financial (e.g., funding of health care programs), technological (e.g., use of computerized order entry systems), and human resources (e.g., staff training and competency) aspects of care.¹⁰⁶⁻¹⁰⁸
- **Process** measures are used to assess activities involved in patient care (e.g., services for prevention, diagnosis, and treatment). These measures may reflect the interpersonal aspects of care/service (e.g., convenience, communication) or technical aspects of care such as the timeliness of diagnosis, appropriateness of therapy, complications, errors, and coordination of care.⁹⁸ In some frameworks, intermediate health outcomes, such as HbA1c as a marker for diabetes control, are included in the process category.¹⁰⁹

Process measures are the predominant quality indicators for inpatient and ambulatory care, although they are applied only occasionally for surgery.¹⁰⁹ The majority of measures target quality of care for specific health conditions, usually those determined to have high disease burden (i.e., morbidity and mortality) in the population, highest rates of utilization of health care services, and highest costs to the health system.¹¹⁰

Laboratory tests are a core component of the condition-related measure sets, i.e., to assess whether or not the patient received the appropriate test.

^P HEDIS consists of 71 measures (e.g., whether or not a patient received beta blocker treatment after a heart attack) across 8 domains of care (i.e., effectiveness, access/availability, satisfaction, health plan stability, use of service, cost of care, informed health care choice, health plan descriptive information). HEDIS is designed to provide purchasers and consumers with the information they need to reliably compare the performance of health care plans.

- **Outcome** measures are used to determine change in patient health status, experiences/satisfaction with care, and cost-related analyses.¹¹¹ Health-related outcome measures include indicators of mortality (e.g., infant death rate), physiologic state (e.g., blood pressure), clinical events (e.g., adverse drug events), symptoms (e.g., level of pain), functioning (e.g., disability), and patients' and clinicians' satisfaction with services (e.g., Consumer Assessment of Health Plan survey).^{112, 113} Outcome measurement increasingly includes assessment of patient quality of life. Laboratory values are important clinical endpoints in outcomes measurement.

The measures are employed to document differences in medical practices, variations in the quality of care, and the efficacy or effectiveness of particular interventions.^{114, 115} In addition, cost-related outcome measures are increasingly applied to determine efficiency and effectiveness in the use of scarce health care resources.

This quality paradigm is an important part of the framework espoused by the IOM⁹ and adopted by AHRQ in the National Health Care Quality Report.^{116, 117} The desirable attributes of a measure are *importance* in the clinical sense to the general population or the quality of care; *scientific soundness* in terms of reliability, validity, and explicitness of evidence base; *usability* in that it has been successfully used in the past and is compatible with other measures; *feasibility* to implement with existing prototypes and considerations pertaining to data availability and cost; *alignment* with leading measure sets; and *comprehensiveness* as part of a measure set that can reflect quality of care for a given condition. (Refer to Appendix A for further information.)

Quality Indicators

Quality indicators are specific attributes of structure, processes, or outcomes whose measurement is capable of providing accurate estimates of the degree to which designated standards were achieved. Although the term "performance indicator" is often used interchangeably with "quality indicator," it is possible to make inferences about performance without making inferences about quality.¹¹⁸ Activity indicators measure the frequency of an event (e.g., screenings for cancer).⁹⁷

Indicators are often based on clinical guidelines and performance standards issued by specialty societies, government agencies, or others, but require greater specificity to be implemented.¹¹⁰ They are designed to convey a finding about the quality of care being provided or health outcomes.¹¹⁹ In particular, they can identify problems that may need to be addressed, usually identified by low indicator scores, statistical outliers, or unexplained variations in care.

To the extent possible, indicators should link processes and outcomes in quality assessment. When cause-and-effect relationships or other associations are established, improvement on process measures can be linked confidently to improvement in patient and population health.¹⁰¹ Linking process measures to outcome measures can demonstrate the capability of clinical approaches to improve patient and population outcomes. Establishing such linkages between indicators and quality or outcomes can be challenging.¹²⁰⁻¹²² Table 5.2 summarizes AHRQ's

⁹ Other components of the framework include the IOM's six aims of quality (safety, effectiveness, patient-centeredness, timeliness, efficiency, equity); the Foundation for Accountability's four domains of consumer needs (staying healthy, getting better, living with illness or disability, and coping with end of life); and the priority areas for quality improvement identified by the IOM, the National Quality Forum, and CMS.

application of performance measure characteristics to evaluate potential quality indicators for its programs as well as that of other organizations.

Indicators can be defined by various metrics such as a rate, ratio, index, or percentage that contributes to qualitative interpretation of a contribution to health care or outcomes.^{123, 124} For dichotomous metrics, an indicator is presented as a proportion where a numerator and denominator are defined,¹²⁵ such as the proportion of diabetic patients who received HbA1c testing. Other metrics may be continuous measures that can be averaged, such as time to an event (e.g., TAT for a clinical chemistry test), a rate defined as a proportion within a given timeframe, or scores on a pain or patient satisfaction scale.

Table 5.2: AHRQ application of criteria for evaluating quality indicators

Quality indicator evaluation framework criteria
1. Importance
<ul style="list-style-type: none"> ▪ Assesses an important leverage point for improving quality; significant to target audiences; impact on health ▪ Opportunity for improvement, considerable variation in quality of care exists ▪ Aspect of quality is under provider or health system control ▪ Should not create incentives or rewards to improve without truly improving quality of care
2. Scientific acceptability
<ul style="list-style-type: none"> ▪ Relationship to quality is based on scientific evidence ▪ Well defined and precisely specified ▪ Valid, measures the intended aspect of quality; accurately represents the concept being evaluated; data sources are comparable ▪ Adequate proportion of total variation is explained by provider performance and amount of variation in measurement is small after provider performance and patient characteristics are taken into account ▪ Reliable, producing the same results a high proportion of time in the same population* ▪ Precise, adequately discriminating between real differences in provider performance and reasonable sample size exists to detect actual differences; captures all possible cases and bias related to case exclusion or limited data is minimal. ▪ Risk adjustment is adequate to address confounding bias
3. Usability
<ul style="list-style-type: none"> ▪ Effective (understandable and clear) presentation and dissemination strategies exist ▪ Statistical testing can be applied to communicate when differences in performance levels are greater than would be expected by chance* ▪ Has been used effectively in the past and/or have high potential for working well with other indicators currently in use ▪ Compelling content for stakeholder decision making
4. Feasibility
<ul style="list-style-type: none"> ▪ Consistent construction and assessment of the measure* ▪ Feasible to calculate; benefits exceed financial and administrative burden of implementation* ▪ Confidentiality concerns are addressed* ▪ Audit strategy can be implemented, quality of data is known*

* Indicates the criterion was not in the initial evaluation framework but has been addressed through incorporation in subsequent work such as quality indicator software.

Source: Guidance for using the AHRQ quality indicators for hospital-level public reporting or payment. Rockville, MD: Agency for Healthcare Research and Quality, 2004.

Collecting and Reporting Data on Performance

Various instruments are employed to collect and report performance data. Some common approaches to data collection include surveys of a targeted population; focus groups; interviews; data abstraction during chart reviews or claims reviews; use of disease registries; reporting through performance monitoring, patient safety, and surveillance systems; and competency assessments. Advances in health information technology are enabling more of these data to be collected electronically. The data derived from measurement often are used to describe patterns of care, detect variations and deficiencies in quality and/or utilization, and perform intra- and interorganizational comparisons. Data may be analyzed and reported at the patient, population, and system levels depending on the purpose of the measurement.^r

Measurement data are reported publicly through assessment tools such as benchmark comparisons, report cards, and balanced scorecards. Benchmark comparisons assess a technical aspect of performance against a designated standard or indicator. Report cards grade performance according to established criteria and indicators. Balanced scorecards give a multidimensional view of performance including technical quality of care, cost, access, patient satisfaction, health status, waiting time in clinics, TAT for laboratory and radiology reports, efficiency, and clinical pathway variances.¹²⁶ Report card data pertaining to laboratory testing are generally limited to utilization. For example, NCQA collects data on whether or not appropriate screening and other laboratory tests for selected medical conditions were performed as an indicator of quality of care. The data are used in annual reports on clinician and health plan performance.¹²⁷

Performance Measurement Initiatives in Laboratory Medicine

A key part of performance improvement in laboratory medicine is the generation of data substantiating the level of practice and defining where practice improvements can have the greatest impact. For clinical and anatomic pathology, this involves collection of data on practices at points along the TTP where risks to quality and safety are likely to arise and where corrective action can result in learning, recovery, and improvement. Historically, this has entailed detecting and correcting errors. However, errors are only one type of shortfall in quality, and the methods used to select quality indicators do not appear to conform to the AHRQ criteria.¹²⁸ Today's quality improvement initiatives have incorporated a more patient-centric, systems-based approach desired by many stakeholders.

As noted above, formal measurement and reporting on quality in laboratory medicine have been limited largely to QC and PT activities to meet regulatory obligations. The effort dedicated to evaluating performance and finding and avoiding errors in the analytic phase has been greater than that for the preanalytic and postanalytic phases. In particular, extensive data on analytic performance has been generated for clinical pathology and certain cytology tests to comply with regulatory and accreditation requirements. These focus on accuracy and consistency of reagents, equipment, and/or methods through internal process control, external PT, and on-site

^r Federal, state, and private sector initiatives in performance measurement are increasingly concerned with data collection at the level of the individual patient, which can be aggregated along three important dimensions: (1) composite measures of the care provided to the individual patient that may document whether that person received recommended care; (2) population-oriented results defined by socioeconomic status, race, and ethnicity; (3) system-oriented results to identify gaps in performance and accountability at the level of the provider, provider group, hospital, and community, and the use of composite measures.¹⁰²

inspections.¹²⁹ CMS and accreditation organizations use the data generated from these activities to determine compliance with standards for analytic processes; accreditation organizations also use the data in training sessions to assist laboratory staff in improving their performance.¹³⁰

Private and public sector organizations have sponsored research and quality improvement efforts to address specific issues in the pre- and postanalytic phases of clinical and anatomic pathology. Most of the studies measure specific variables (e.g., patient and specimen identification errors, results reports correction rates) in order to discern ways to reduce errors, improve safety, and identify best practices.^{41, 131-133} These research studies were not conducted with indicators that have been evaluated against the AHRQ criteria presented previously, and are not included in AHRQ's National Quality Measures Clearinghouse. Nevertheless, these studies may offer useful opportunities to assess the characteristics of quality indicators and practices that warrant further research and development. Brief descriptions of the studies undertaken by CAP through its Q-Probes and Q-Tracks programs, The Joint Commission's initiatives, and activities of other organizations and government agencies are provided below.

College of American Pathologists

CAP launched the Q-Probes program in 1989 to establish performance measures for laboratory quality.¹³⁴ Targeted short-term studies in these programs assess the effects of specific practices and attempt to establish benchmarks for measuring performance. Typically completed within 4 months, these studies aim to provide a snapshot of participants' performance on QA variables, which can be used for external peer-comparison, goal setting, and improvement. Most of the variables are process-oriented, although a few are structural or outcome oriented. To date, CAP has published more than 120 studies involving Q-Probes in peer-reviewed journals on a limited number of indicators and topics. As noted above, they have not been evaluated against AHRQ's criteria for inclusion in the National Quality Measures Clearinghouse.¹³⁵

The same holds true for the CAP Q-Tracks program initiated in 1998 for longitudinal tracking of laboratory performance on key indicators. The program was designed to satisfy accreditation requirements for continuous monitoring and benchmarking in clinical and anatomic pathology. In 1999, the Q-Tracks program was approved by The Joint Commission for inclusion in its ORYX^s quality indicator monitoring system. Q-Tracks provide continuous monitoring of 12 indicators (see Appendix B) and variables previously defined in Q-Probes studies (e.g., patient identification accuracy, blood culture contamination, laboratory specimen acceptability). Users subscribe to the program for a 12-month period during which they are provided with quarterly reports about their performance as well as the practices and policies of other participants associated with improved performance based on the non-standardized, self-reported data.¹³³ Since the program's inception, about one-third of Q-Tracks indicators have been retired.^t Given current efforts to establish national, standardized performance measures across the health system that can be used for external public reporting, the applicability of CAP Q-Tracks indicators remains unclear. CAP measures were designed for internal process improvement purposes, and may continue to be useful in this regard.

^s ORYX is a performance monitoring system developed by The Joint Commission. It was designed to collect data on standardized core and non-core performance measures approved by The Joint Commission. In order to maintain Joint Commission accreditation, hospitals are required to collect and submit data on some of the measures.

^t Since the inception of Q-Tracks, 17 indicators have been developed; 12 are in use and 5 have been retired.

Many institutions participating in Q-Probes and Q-Tracks studies have documented performance improvements. Even so, such improvements were based largely on self-reported, longitudinal data of participating institutions, as opposed to comparisons to control groups, characteristic of more rigorous scientific studies.^{133, 136, 137} Another factor that may have a modest effect on performance comparisons is the degree of variability among participating laboratories in such aspects as test menus, employee skill levels, and utilization by physicians. CAP programs adjust for some of the differences by restricting interlaboratory comparisons to peer groupings of laboratories that are similar with respect to unmanageable characteristics. Even so, the adjustments are likely insufficient to counter the lack of standardization, the most relevant issue pertaining to validity of laboratory performance measures. As a result, laboratories participating in CAP studies are reporting error rates and other measures that may have been determined differently. This may in part explain the large variation in error rates among the various studies.

There appear to be no published studies evaluating CAP or other measures according to criteria appropriate for quality indicators (e.g., health importance, scientific acceptability, usability, feasibility) as defined by AHRQ. Similarly, the CAP measures do not appear to have been assessed for generalizability across laboratory settings or studied for applicability and feasibility in POLs.¹³⁸ Although CAP measures were not designed for the purpose of accountability and public reporting, they have established face validity, feasibility for data collection, and that they are actionable.¹³⁸ The CAP measures are in need of further testing to ascertain their validity, accuracy and reliability for potential use in external reporting.

Along similar lines, in 1993, CAP initiated the Laboratory Management Index Program, a fiscal management tool that provides peer comparisons to assist laboratories with the annual budget process, contract negotiations, and daily operations management.^{139, 140} The program uses management ratios and total standard billable tests as performance indicators to assess the three main management-related factors affecting laboratory performance: productivity, utilization, and cost-effectiveness. Their favorable impact notwithstanding, CAP indicators of management quality also are based on self-reported, non-standardized data.

The Joint Commission

In addition to the ORYX monitoring system, The Joint Commission issues National Patient Safety Goals (NPSGs) annually to advance specific improvements in patient safety by highlighting problematic areas and prescribing expert-based solutions.¹⁴¹ Four of the NPSGs for health care organizations apply directly to the laboratory (see Table 5.3). For example, based on expert opinion, The Joint Commission states that the goal of improving patient identification accuracy can be reached by using two patient identifiers when administering medication, collecting blood samples, or providing other treatments. It suggests not using the patient's room number or physical location for identification, labeling containers for blood and other specimens in the presence of the patient, and maintaining a sample's identity throughout all stages of laboratory testing as methods to reach this goal.¹⁴² Because these actions recommended by The Joint Commission are considered to be viable means of reducing errors, they warrant further study and evaluation.

A few studies that examined areas important to The Joint Commission's work cite modest decreases in error rates based on high-level interventions; however, it is difficult in these studies to establish causal relationships or evaluate an explicitly defined measure. For example, from 2002 to 2004, UCLA Clinical Laboratories studied patient identification and specimen labeling

errors, a priority area for The Joint Commission. Laboratories implemented three patient safety improvement strategies: (1) increased the number of phlebotomists on staff and expanded services to 24 hours daily, (2) implemented an online electronic event reporting system, and (3) instituted an automated processing system.¹⁴³ Errors associated with mislabeled specimens decreased significantly. In another example, three microbiology laboratories assessed the impact of requiring “read-back” from the recipient of telephone results reports and noted reduced risk of medical errors.¹⁴⁴ The measures used in such studies are not necessarily validated, and it is difficult to determine which of the interventions, if any, had a causal effect on error rates, or whether there were other factors that influenced the observed changes in error rates.

Some researchers have experienced challenges when incorporating NPSGs into their information systems. For example, staff at Massachusetts General Hospital analyzed its reporting of critical values, i.e., those laboratory results indicating the patient is in imminent danger and requires immediate initiation of appropriate therapy. The hospital uses computer applications (e.g., CPOE, clinical decision support systems, electronic results reporting) that apply rule-based logic to determine which values are truly critical and which are within acceptable reference limits for certain medical conditions and given the patient’s previous test results. However, the researchers concluded that these more nuanced approaches to critical value reporting are constrained by the Joint Commission’s requirement that all critical values be reported.¹⁴⁵

In addition, results of a recent study funded by the CDC may contradict current and long-held conventional wisdom underlying critical values reporting. For example, preliminary findings presented at the September 2007 CLIAC meeting indicate that reporting of non-critical potassium values (within a certain range) had a greater impact on patient treatment and outcomes than critical values.¹⁴⁶ This implies the need to re-evaluate traditional beliefs about effective measures, practices and requirements to improve safety and quality.

Table 5.3: 2008 National Patient Safety Goals, Laboratory Services Program

Goal 1	Improve the accuracy of patient identification. (Introduced in 2004)
1A	Use at least two patient identifiers when providing care, treatment or services.
1B	Prior to the start of any invasive procedure, conduct a final verification process (such as a “time out”) to confirm the correct patient, procedure and site, using active—not passive—communication techniques.
Goal 2	Improve the effectiveness of communication among caregivers. (Introduced in 2004)
2A	For verbal or telephone orders or for telephonic reporting of critical test results, verify the complete order or test result by having the person receiving the information record and “read-back” the complete order or test result.
2B	Standardize a list of abbreviations, acronyms, symbols, and dose designations that are not to be used throughout the organization.
2C	Measure and assess, and if appropriate, take action to improve the timeliness of reporting, and the timeliness of receipt by the responsible licensed caregiver, of critical test results and values.
2E	Implement a standardized approach to “hand off” communications, including an opportunity to ask and respond to questions.
Goal 7	Reduce the risk of health care-associated infections. (Introduced in 2004)
7A	Comply with current World Health Organization (WHO) Hand Hygiene Guidelines or Centers for Disease Control and Prevention (CDC) hand hygiene guidelines.
7B	Manage as sentinel events all identified cases of unanticipated death or major permanent loss of function associated with a health care-associated infection.

Goal 13	Encourage patients' active involvement in their own care as a patient safety strategy. (Introduced in 2008)
13A	Define and communicate the means for patients and their families to report concerns about safety and encourage them to do so.

Note: Gaps in the numbering indicate that the Goal is inapplicable to the program or has been "retired," usually because the requirements were integrated into Joint Commission standards.

Source: 2008 National Patient Safety Goals, laboratory services program. Oakbrook Terrace, IL: The Joint Commission, 2007. (Accessed November 14, 2007, at http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/08_lab_npsqs.htm.)

Other Accreditation Organizations and Government Initiatives

While other laboratory accrediting organizations do not collect and evaluate specific measures in the manner of CAP or The Joint Commission, some are developing alternative methods of tracking performance. In 2007, ASHI developed an online database of the deficiencies reported from inspections to assist laboratories it accredits with fulfillment of CMS requirements. AABB requires blood banks to implement QMS with internal processes for monitoring and addressing transfusion practices as a condition for accreditation. Monitored performance indicators are related to ordering practices, patient identification, sample collection and labeling, infectious and noninfectious adverse events, near-miss events, usage and discard practices, appropriateness of use, blood administration policies, ability to meet patient needs, and compliance with peer-review recommendations.⁴²

Several federal health agencies have undertaken efforts to support development of laboratory performance measures, including AHRQ, CDC, and CMS. AHRQ funded the creation of a national anatomic pathology errors database in 2002 to track the frequency and severity of errors detected by cytologic-histologic correlation for both gynecologic and nongynecologic cytologic and histologic diagnoses.¹⁴⁷

CDC launched a project in 2006 to develop an evidence-based process to identify and evaluate laboratory medicine practices and to recommend "best practices." The first phase of the project (2006-2007) completed initial development of the Laboratory Medicine Best Practices review and evaluation methods, and the second phase (2007-2008) is intended to refine and improve methods to review these practices, including development of a new investigational component to obtain unpublished studies to supplement the available published studies. The investigational component will rely on establishing a network of laboratories who have previously completed practice evaluations to pilot test the process. These methods are being developed under a contract with Battelle Memorial Institute with the guidance of a 14-member multi-disciplinary expert advisory workgroup that will also make recommendations relating to an organizational structure and other requirements for future implementation and sustainability of a laboratory medicine best practices evaluation and identification process, among other things.^u CDC also announced a funding opportunity in 2007 to evaluate clinical laboratory practice by developing evidence-based laboratory medicine quality and performance measures associated with the pre- and postanalytic

^u Specifically, phase I of the project (2006-2007) established definitions of best practices, developed inclusion and exclusion criteria for candidate practices, created a classification scheme, established methods for a systematic review, created a framework for making best practices recommendations, conducted a proof of concept exercise, and defined strategic organizational and implementation constructs. Phase II (2007-2008) aims to refine and develop process review and evaluation methods, pilot test the process, develop and test the investigational component, and evaluate alternative organizational mechanisms for implementing the process.

stages of the TTP. These measures are to be based on important gaps and opportunities for improvement in laboratory medicine quality consistent with available evidence and national health care priorities to improve public health.¹⁴⁸ To date, cooperative agreements have been awarded to the following entities to develop measures for the pre- and postanalytic stages:

- Texas Department of State Health Services – linking the quality of patient care with the quality of pre- and postanalytic stages of the newborn screening process
- Kaiser Permanente Center for Health Research Research Institute – evaluating laboratory medicine quality in chronic kidney disease associated with improved patient outcomes
- University of Colorado – associated with specific pathology and laboratory processes affecting clinical and patient-related outcomes¹⁴⁹

CMS maintains the OSCAR database of information collected by surveyors during laboratory inspections.¹⁵⁰ Another database houses information on laboratory PT results. The database systems are not accessible to the public; however, CMS will provide information by request. While CMS has not undertaken performance measurement initiatives directly assessing the quality of laboratory medicine, it recently launched the Physician Quality Reporting Initiative, which provides a financial incentive for physicians to participate in this voluntary quality reporting program. For example, physicians reporting from July 1 through December 31, 2007 were eligible for an incentive payment in 2008. One of the measures pertains to physician ordering of laboratory tests.¹⁵¹

A Model for a National Laboratory Performance Measurement System

In 2006, CDC funded an initiative led by Raj Rehal in association with the National Quality Forum (NQF) to develop a framework for collecting, measuring, and reporting performance data on laboratory tests associated with priority health conditions, processes of care, and infrastructure.¹³⁸

As a first step, the study examined the strength of evidence for health condition-specific guidelines and associated laboratory-related performance measures recommended by professional societies.^v The priority health conditions include diabetes, obesity, heart failure, ischemic heart disease, stroke, kidney disease, hypertension, depression and mental illness, pneumonia, cervical and colon cancer, pregnancy and childbirth, asthma, and patient safety. For example, the clinical guidelines published in the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* recommended a set of laboratory tests prior to initiating therapy: blood glucose, hematocrit, potassium, creatine and estimated glomerular filtration rate, calcium, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and urinalysis. Tests for urinary albumin excretion or albumin/creatinine ratio are described as optional.¹⁵² However, according to the NQF study, laboratory-based performance measures to assess the quality of laboratory testing and services have not been specified by professional societies. The lack of such measures was consistent across each health condition reviewed in the study.

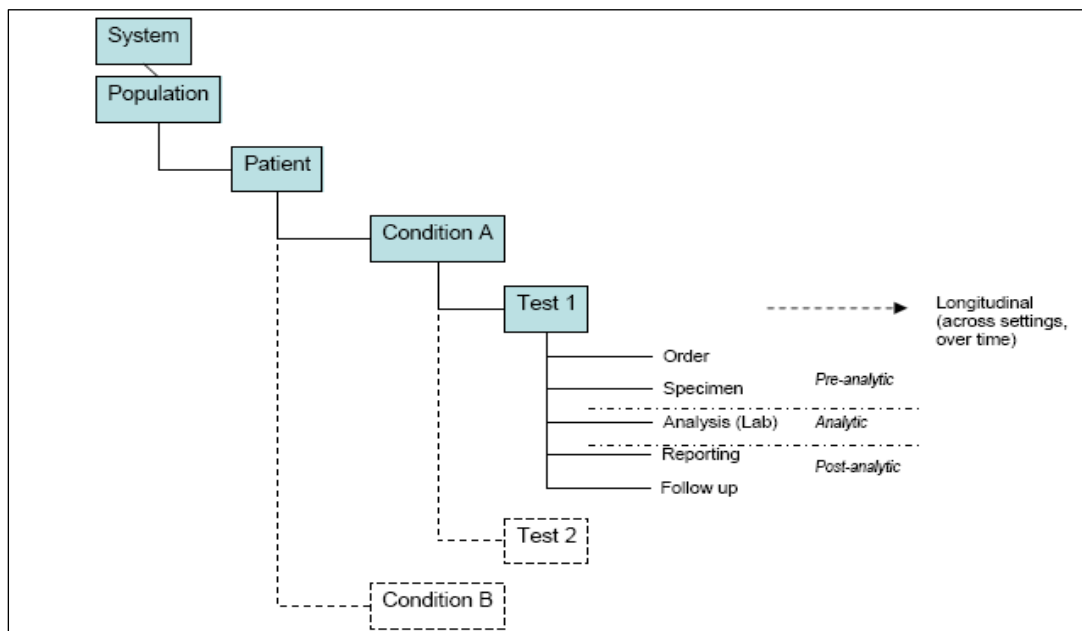
^v The professional societies included in the NQF study are: the American Diabetes Association, American College of Cardiology, American Heart Association, The Joint Commission, Hospital Quality Alliance, National Committee for Quality Assurance, Physician Consortium for Performance Improvement of the American Medical Association.

Subsequent to this review, NQF commissioned the development of a framework based on the structure established for the AHRQ *National Health Care Quality Report*. In addition, the framework is consistent with the IOM reports, *Priority Areas for National Action: Transforming Health Care Quality* (2003) and *Performance Measurement: Accelerating Improvement* (2006). NQF drew from the design principles espoused in the latter report, including:

- (1) Comprehensive measurement that advances the six aims identified in the IOM *Quality Chasm* report
- (2) Longitudinal measurement that spans care settings over time
- (3) Individual patient-level, population-level, and system-level measurement instead of a provider-specific or silo-of-care focus
- (4) Shared accountability instead of focusing on individuals' actions

The framework is depicted in Figure 5.1. The intention of this approach is to address needs of multiple stakeholders and link evidence-based laboratory tests with national initiatives in performance measurement. It allows for data collection on specific tests associated with priority conditions at the level of the individual patient, which can be rolled up to the levels of the populations and systems. The framework addresses laboratory performance in key dimensions of the TTP: ordering, specimen, analysis, reporting, and follow-up.

Figure 5.1: A Framework for performance measurement in laboratory medicine.



Source: Behal R. Identification of performance measures of importance for quality in laboratory medicine. Washington, DC: National Quality Forum, 2007.

The framework was designed with flexibility for evaluation of both clinical and anatomic pathology testing processes. However, several limitations of the current framework have been identified.¹³⁸ First, all but one of the laboratory tests associated with the health conditions are clinical pathology tests. The exception is cancer screening for women, which includes gynecologic cytology tests. Anatomic pathology tests may not be sufficiently represented. However, the extensive research on

anatomic pathology tests associated with cancer could provide sufficient evidence base for selecting specific indicators. Second, there are few, if any, measures for children with special needs, frailty due to old age, mental illness, self management, care coordination, care at the end of life, and pain management. Third, few laboratory tests that are considered evidence-based are included in the performance measures. Fourth, measures to evaluate appropriateness of laboratory tests (e.g., overuse, underuse, misuse) have not been developed. Generally, HEDIS and other condition-related measures are used as substitutes to determine underuse; only a few studies of clinical decision support systems relative to physician test ordering and payer utilization reviews have been employed to assess overuse or misuse.^{153, 154}

Current Measures Used in Laboratory Medicine

Specific areas for evaluation and development of performance measures in laboratory medicine are depicted in Figure 5.2. Structural measures are affiliated with core environmental factors that may affect quality. Process measures assess the preanalytic, analytic, and postanalytic components of the TTP, also considered to be the critical control points at which errors and other problems can be corrected and/or prevented. Outcome measures tie the laboratory testing process to patient health and costs of care. The facets identified in the structural, process, and outcome categories may be used for internal or external assessment and quality improvement programs, as depicted by the arrows in the diagram. Each structural, process, and outcome measure also may be evaluated independently. The status of the measures is discussed more fully in the next section. Appendix B provides examples of specific structural, process, and outcome measures identified in the literature.

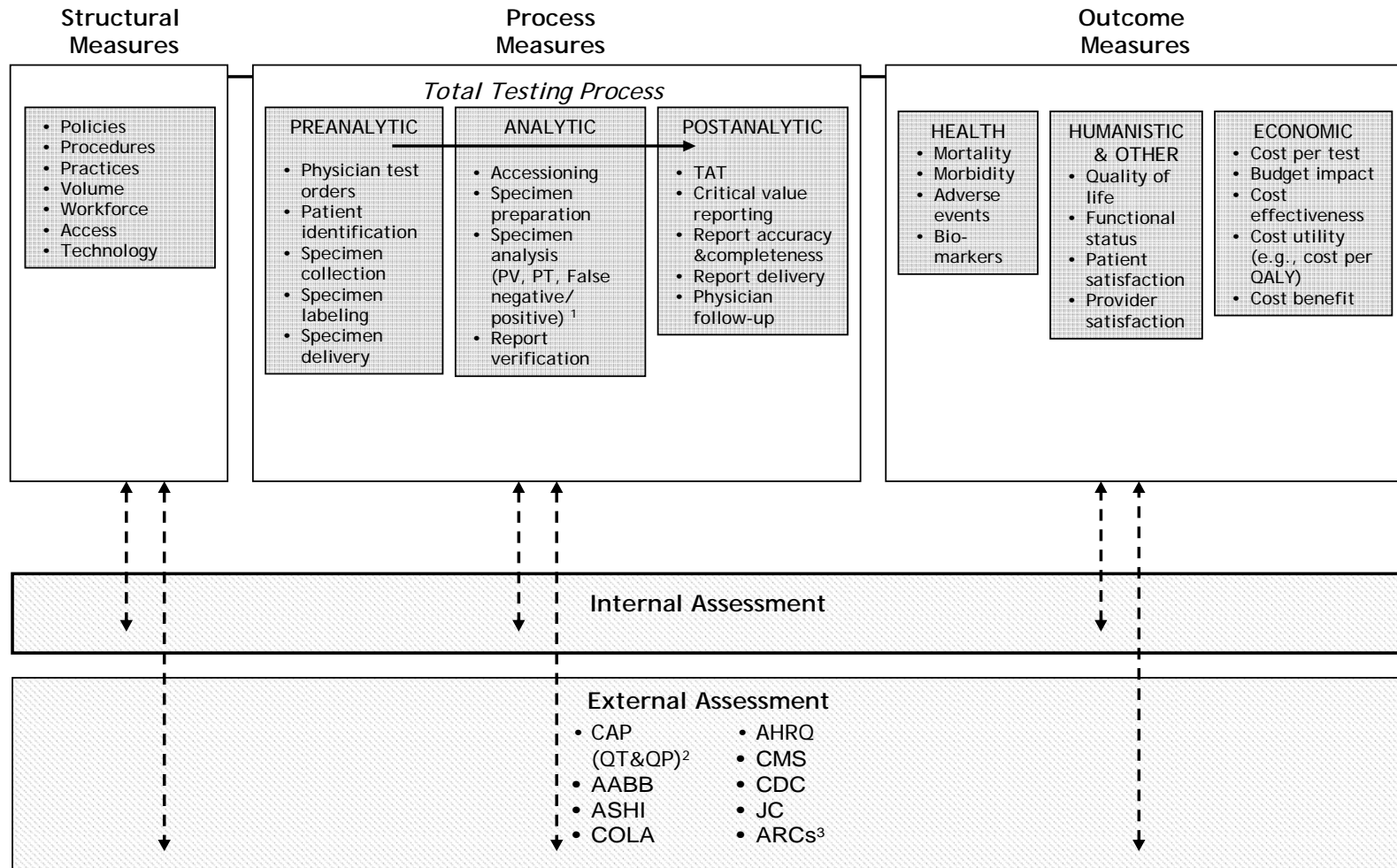
Structural Measures

With the exception of PT, most of the regulatory provisions to support quality systems mandated under CLIA are structural requirements. The majority of provisions outline basic requirements for policies, procedures, and documentation that must be in place for preanalytic, analytic, and postanalytic phases as a condition of certification/accreditation.

A few studies have examined other structural measures such as workforce productivity and staffing ratios and use of web-based error reporting systems. A study examined the impact of workforce on quality and factors associated with favorable staffing ratios. They measured productivity of technical staff and management staff span-of-control ratios. The study found wide variability in staffing levels among institutions, suggesting opportunities to improve staff productivity in many facilities.¹⁵⁵ In studies of health or laboratory information technology infrastructure, basic metrics are developed to determine the rates of implementation, often delineated by initiation of specific software programs, cross-departmental data exchange networks, and database systems.⁹

Another study of POCT systems evaluated the implementation of specific error-prevention systems and safeguards, most of which are structural factors influencing quality because they are associated with technology systems and workforce training. The study produced a summary of actions for preventing medical errors: (1) adopt operator certification and validation in POCT testing; (2) implement security, validation, performance, and emergency override systems on existing and new devices; (3) require flexible, user-defined error prevention system options on instruments as a prerequisite to federal licensing of new diagnostic tests and devices; (4) integrate connectivity standards for bidirectional information exchange; (5) preserve fast TAT of POCT

Figure 5.2: Diagram of Categories for Performance Indicators in Laboratory Medicine



¹ PV-Predictive Value, PT-Proficiency Testing

² QT-QTracks, QP-QProbes

³ ARCs-Academic research centers

results; (6) monitor invalid use, operator competence, quality compliance, and other performance improvement indices to reduce errors.¹⁵⁶

Most structural measures are insufficient or too general to serve as indicators of performance or quality of care.¹¹⁶ Links between structure and processes of care and structure and outcomes tend to have adequate evidence-based support only in limited areas (e.g., mortality at high volume hospitals is up to 10% lower than at lower volume facilities).^{157, 158} Furthermore, structural measures have limited use outside the hospital setting, are not readily actionable, and do not adequately discriminate performance among individual clinicians. With the exception of laboratory medicine, national initiatives assessing quality have shifted focus to outcome-validated process measures and disease- or process-specific outcome measures.¹¹⁶

Process Measures

Process-related performance measures in laboratory medicine are associated with the TTP as presented in Figure 5.2 and Appendix B, and discussed at length in the previous chapter of this report (Quality and the Total Testing Process). Thus far, the non-standardized methods employed to evaluate quality and estimate error rates have formed a growing body of research on all three phases of the laboratory testing cycle. Error rates and a few other dimensions for certain aspects of pre- and postanalytic phases of testing have been evaluated through the CAP programs and other research studies.¹⁵⁹ Studies of the preanalytic processes typically measure performance via error rates tied to specimen collection (e.g., phlebotomy success, specimen acceptability, specimen contamination), followed by specimen labeling (e.g., ABO typing or various errors), and patient identification (e.g., wristband error).¹⁶⁰⁻¹⁶⁵ A few published studies have examined errors associated with clinician ordering, in terms of the accuracy and completeness of requisition slips and/or the appropriateness of test orders (e.g., duplicate orders).¹⁶⁶

For postanalytic processes, performance measures have targeted measurement of TAT in various capacities (i.e., routine TAT, critical value TAT, and stat TAT) and report accuracy (e.g., completeness of descriptors, discrepancies, amended report rates).^{134, 167-172} More recent studies measured interpretive consultation rates and report delivery errors.¹⁷³⁻¹⁷⁵ Very few studies have examined appropriate interpretation of laboratory test results and ensuing laboratory-driven clinical/preventive actions and related patient outcomes.

Most published studies of preanalytic and postanalytic factors calculated total error rates, but not all collected sufficient data to determine the nature of and specific causes of the errors for identification of potentially effective quality improvement strategies. For example, in a Q-Tracks study of specimen acceptability, the overall specimen rejection rate served as the primary performance indicator, with secondary data submitted on specific reasons for rejection such as for clotted specimen, container leaking, specimen contamination, hemolyzed specimen, insufficient volume, tube over/underfilled, specimen lost/not received, and improper container.¹³³

In contrast to pre- and postanalytic measures, analytic phase process measures are better developed and accompanied by a stronger evidence base, such as for error rates as measured by internal QC and PT. Routine QC checks can provide important data about the potential for accuracy versus the potential for error in testing and sources of variation for each analyte. These data are tracked over time to evaluate within-laboratory factors as well as to ensure achieving specified levels of performance. Similarly, PT is a standard measure of analytic performance for

purposes of external evaluation and regulatory oversight. PT data, including root causes of errors, serve as key measures to provide insight into how well a laboratory is performing compared to other laboratories. (Refer to the Federal Regulatory Oversight chapter of this report for additional discussion of QC and PT.)

Figure 5.3 summarizes the process-related performance measures. Experts participating in CDC's Institute for Quality in Laboratory Medicine in 2005 expanded on the measures initially employed by CAP through its Q-Tracks program. CDC recently undertook an evaluation of process measures published in the literature and found a general lack of evidence supporting health importance, scientific soundness, relevance, and usefulness.¹⁷⁶ Significant variability and gaps were identified in terms of standardized terminology, measurement specifications, data collection methods, and relationships to process, clinical, health, and economic outcomes. For example, although specimen adequacy can affect the accuracy and usefulness of laboratory test results, there is no standard definition or measure to evaluate adequacy aside from overall rejection rates.^{160-162, 177} A systematic study that relates specimen adequacy or rejection to other outcomes has not been conducted.

When CDC assessed the process measures for their applicability to the IOM's six domains of health care quality, they fell short, especially in the areas of patient-centeredness and equity. Other areas not adequately addressed include laboratory testing for preventive care and the use of health information technology (e.g., order entry and decision support) as a tool to enhance quality and safety.¹⁷⁸⁻¹⁸¹

Overall, an important limitation of current laboratory process measures is the variable extent to which they link to outcome measures, along with sample size constraints and potential to be affected by such confounding factors as patient compliance. Some measures can be linked to outcomes (e.g., false-positive and false-negative results) supported with scientific evidence, while the relationship for others is weak (e.g., patient identification, specimen collection, TAT).¹⁰⁹ Additional work is needed to standardize the indicator metrics (i.e., numerators and denominators, or other methods for calculation) for pre-and postanalytic process-related performance measures. As most research to date has focused on the needs of larger, hospital-based laboratories, further research also is needed to ascertain the specific challenges that smaller POLs may confront when implementing process-related performance measurement and quality improvement programs.

In efforts to address these issues, the Behal/NQF framework presents a different approach to performance measurement. The particular indicators for the preanalytic and postanalytic phases of the total testing process have yet to be evaluated using AHRQ criteria; however, the paper identified general areas for additional evaluation that included test ordering, specimen collection, proficiency testing, results reporting, and physician actions. Rather than measure performance in the broad sense, evaluations are proposed based on laboratory tests associated with the national priority health conditions.¹³⁸ This approach may facilitate understanding of the relationships between laboratory testing and outcomes.

Table 5.3: Potential Areas for Performance Measure Development and Standardization

CAP (2002), Howanitz (2005), and IQLM (2005)	NQF (2007)
<p>Preanalytic</p> <ul style="list-style-type: none"> ▪ Test order accuracy and appropriateness ▪ Patient identification ▪ Specimen rejection (chemistry & hematology) ▪ Blood product wastage(transfusion medicine) ▪ Blood culture contamination (microbiology) ▪ Adequacy of specimen container information <p>Analytic Phase</p> <ul style="list-style-type: none"> ▪ Cervical cytology-biopsy correlation ▪ Accuracy of POCT ▪ Proficiency testing <p>Postanalytic Phase</p> <ul style="list-style-type: none"> ▪ Test TATs (chemistry & hematology) ▪ Critical values reporting ▪ Clinician follow-up (abnormal Pap test, hypercalcemia) ▪ Clinician satisfaction (all lab disciplines) <p>Additional special areas</p> <ul style="list-style-type: none"> ▪ Diabetes monitoring ▪ Hyperlipidemia screening ▪ Timing of therapeutic drug monitoring ▪ Intraoperative consultations 	<p>Preanalytic Phase</p> <ul style="list-style-type: none"> ▪ Test order ▪ Specimen collection <p>Analytic Phase</p> <ul style="list-style-type: none"> ▪ Specimen analysis (proficiency testing) <p>Postanalytic Phase</p> <ul style="list-style-type: none"> ▪ Results reporting (TAT, critical values) ▪ Physician follow-up <p>Specific health condition-related tests</p> <ul style="list-style-type: none"> ▪ Diabetes ▪ Obesity ▪ Heart failure ▪ Ischemic heart disease ▪ Stroke ▪ Kidney disease ▪ Hypertension ▪ Depression and mental illness ▪ Pneumonia ▪ Cervical and colon cancer screening ▪ Pregnancy and childbirth ▪ Asthma ▪ Patient safety

Sources: Zarbo RJ, Jones BA, Friedberg RC, Valenstein PN, Renner SW, Schiffman RB, et al. Q-tracks: a College of American Pathologists program of continuous laboratory monitoring and longitudinal tracking. Arch Pathol Lab Med 2002;126(9):1036-1044.

Howanitz PJ. Errors in laboratory medicine: practical lessons to improve patient safety. Arch Pathol Lab Med 2005;129:1252-1261.

Hilborne L. Quality Indicators Workgroup presentation. 2005 Institute for Quality in Laboratory Medicine Conference: Recognizing Excellence in Practice. April 29, 2005. Atlanta, GA: Centers for Disease Control and Prevention, 2005.

Behal R. Identification of performance measures of importance for quality in laboratory medicine. Washington, DC: National Quality Forum, 2007.

Outcome Measures and Indicators

As is the case for other types of health care interventions, laboratory testing can be assessed for its impact on health outcomes, humanistic outcomes, and economic outcomes.¹³⁸ Health outcomes include mortality, morbidity, adverse events, and biomarkers (e.g., laboratory values). Some biomarkers are used as intermediate or surrogate outcomes, in that they are known to be predictive of health outcomes. Humanistic outcomes typically include quality of life, functional status, patient satisfaction, and other patient-reported outcomes. Among the many types of economic outcomes are cost per test, patient, treatment and episode of care; budget impact; and analyses of tradeoffs, including cost-effectiveness, cost-utility, and cost-benefit analysis.

Outcome studies in laboratory medicine address questions of the form: *Is use of test X associated with outcome Y?*¹⁸² For example, does fecal occult blood testing decrease the incidence of colorectal cancer? These studies have focused on the usefulness of screening tests in the prevention and early detection of disease, such as various cancers, and comorbidities associated with certain conditions (e.g., diabetes), among others.¹⁸³⁻¹⁸⁵ For example, a systematic review examined the evidence that screening and earlier treatment are effective in reducing morbidity and mortality associated with Type II diabetes. The review found that, for high-risk populations, screening tests can detect diabetes in its preclinical phase, and that over the 10-15 years after clinical diagnosis, tight glycemic control can improve patient outcomes by reducing the risk for blindness and end-stage renal disease.¹⁸⁶ The USPSTF relies on outcome studies of this nature to develop evidence-based guidelines for priority health conditions.

Outcome studies also have identified adverse events arising from incorrect test results. These studies assess the relationships between analytic accuracy (i.e., false-negative or false-positive results) to detrimental effects on patient health (e.g., disease progression that would have otherwise been discovered or unnecessary surgery).¹⁸⁷⁻¹⁸⁹ An example concerns a study in which 12 women were diagnosed with having postgestational choriocarcinoma on the basis of false-positive test results for human chorionic gonadotropin.¹⁹⁰ The errors had adverse consequences for patient outcomes, as most of these women were subject to unnecessary surgery and chemotherapy.

Other outcome studies examined provider or patient satisfaction with aspects of care. For example, an ongoing Q-Tracks study is using two high-level measures, i.e., overall patient satisfaction score and percentage of patients more than satisfied, to assess satisfaction with outpatient specimen collection.¹⁹¹ A Q-Probes study relied on more detailed data collection to assess patient satisfaction, including aggregate scores, percentage of excellent/good ratings, below average/poor ratings, and satisfaction for 10-13 specific aspects of laboratory service.¹⁹²

While patient outcome studies are gradually becoming more common in laboratory medicine, they are not yet a regular part of ongoing quality improvement practices. Laboratory-related outcome measurement is underused for several reasons, including the high cost of capturing outcomes data, lack of standardization of data collection and reporting methods, and lack of agreement regarding appropriate analysis of data (e.g., whether or not to risk-adjust data). Furthermore, outcome measurement can be severely constrained by sample size, test results missing from patients' medical records, limited risk adjustment capability with data abstracted from administrative records, and higher cost to abstract data from medical records.¹⁰⁹ Other problems consistently identified in the literature include the inability to conceal the identity of

tested versus non-tested patients, the relative remoteness of an outcome to the test itself, and the number of patients or volunteers required for a study to achieve statistical significance.^{114, 115, 182, 193}

Intermediate outcomes association with biomarkers, such as HbA1c and glucose for diabetes, are generally easier to measure than patient outcomes to assess the impact of health care interventions and thus, are more commonly used. A biomarker is a variable that is objectively measured as an indicator of normal biological processes, pathogenic processes, or pharmacological response to a therapeutic intervention. A surrogate (or intermediate) endpoint is a biomarker or physiological marker that is intended to act as a substitute for or predict a patient outcome. They are relatively quickly or easily measured and their use is based on evidence that it is a reliable predictor of the patient outcome of interest. Certainly, some biomarkers are better predictors of patient outcomes than others. Examples are: blood pressure or cholesterol levels for predicting the incidence and course of cardiovascular disease, T-cell counts for predicting survival of AIDS patients, and PSA levels for predicting the incidence and course of prostate cancer.

Cost-related Measures and Indicators

Cost-related outcome assessment is growing in use, although relatively little research has been conducted as pertains to laboratory testing.^{102, 194} An example of such studies in laboratory medicine is one that assessed the cost-effectiveness of periodic, population-based dipstick screening for early detection of urine protein in adults with neither hypertension nor diabetes and in adults with hypertension. Using a Markov^w decision analytic model, the study compared a strategy of annual screening with no screening (usual care) for proteinuria at age 50 years followed by treatment with an angiotensin-converting enzyme inhibitor or an angiotensin II-receptor blocker. Among the findings, for persons with neither hypertension nor diabetes, the cost-effectiveness ratio for screening vs. no screening (usual care) was an unfavorable \$282,818 per QALY,^x but \$53,372 for persons age ≥ 60 years, and a highly favorable \$18,621 per QALY for persons with hypertension. The analysis showed that factors that tend to improve cost-effectiveness of screening for the general population include a greater incidence of proteinuria, age >60 years at screening, and lower frequency of screening. The investigators concluded that early detection of urine protein to slow progression of chronic kidney disease and decrease mortality is not cost-effective unless selectively directed toward high-risk groups (older persons and persons with hypertension) or conducted at an infrequent interval of 10 years.¹⁹⁸

Another study modeled the cost-effectiveness of routinely using tandem mass spectrometry to screen newborns for inborn errors of metabolism based on data from a large health maintenance organization. Depending upon assumptions in three scenarios, the cost per QALY ranged from \$736 to \$11,419. These findings led the investigators to conclude that costs per QALY saved by

^w The Markov model is a statistical state-transition model in which the transition probabilities depend only on the current state and not on previous states or the pathway by which the state was entered.¹⁹⁵

^x The QALY is a composite unit of length of life and utility for particular levels of quality of life. Ones' utility for quality of life is measured on a scale from 1.0 (utility for perfect health) to death (0.0). For example, 1 year of life lived in perfect health (utility of 1.0) health yields 1.0 QALYs, 0.5 years of life lived in perfect health yields 0.5 QALYs, and 1 year of life lived in a lesser state of health (e.g., bedridden) with a utility of 0.5 is also equivalent to 0.5 QALYs. The QALY may be used as the unit of patient/user outcomes in a cost-effectiveness (or cost-utility) analysis.^{196, 197} In developed economies, a health care intervention is considered to be cost effective if its cost per QALY falls under a certain threshold, (e.g., \$30,000 per QALY or \$50,000 per QALY or \$100,000 per QALY). In the U.S., such thresholds are generally regarded as informal only, and do not have bearing on payment decisions.

tandem mass spectrometry for inborn errors of metabolism compare favorably with other mass screening programs such as for breast and prostate cancer.¹⁹⁹

Several studies have examined the cost of POCT relative to central laboratory testing using metrics such as cost-per-test (including estimates for the cost of equipment, supplies, labor, and other variables) and laboratory test TAT.^{200,201} For example, a study reported in 2004 compared the analytical costs of central laboratory glucose testing and semiautomated bedside glucose testing (BGT) among 445 institutions enrolled in the Q-Probes program. Results showed different distributions of costs across three main types of sites. The median (10th-90th percentile range) analytical costs per glucose test were \$1.18 dollars (\$0.36-\$5.59) for central laboratories, \$1.96 (\$0.77-\$9.51) for high-volume BGT sites, and \$4.66 (\$1.02-\$27.54) for low-volume BGT sites. In addition to being higher than costs for central laboratories, costs for BGT were highly variable and dependent on volume. The investigators observed that data that would be used for financial justification for BGT were widely aberrant and in need of improvement.²⁰²

CONCLUSIONS

To achieve consistently high levels of quality in laboratory medicine requires moving beyond analytic-focused QC and PT activities to more comprehensive, systematic approaches to quality management that support the integration of preanalytic, analytic, and postanalytic components, external assessment and accountability. An important tool of QMS and improvement programs is the use of performance measurement to assess achievement of quality standards for structural features that support quality, processes of care, and health outcomes.

- Relative to the five levels of quality,^y most health care organizations, including laboratories, are operating at or below the stage of QA, although some have implemented and are working successfully at the level of QMS. Organizations that implement QMS are better equipped to reduce or eliminate errors, meet customer needs, score well on government or accreditation assessments, and maintain quality objectives. CLSI and ISO^z have developed standards for QMS.
- By adopting ISO 9000 standards, QMS has been most broadly adopted in transfusion medicine to meet FDA requirements for Current Good Manufacturing Practices and Quality Assurance Guidelines. Use of ISO 9001:2000, ISO 15189, and CLSI guidelines in laboratory medicine has accelerated in recent years as CMS and laboratory accreditation organizations incorporate QMS-related standards into their regulatory requirements.
- CQI, Toyota “lean” production, Six Sigma, and FMEA are strategic tools for implementing QMS that are realizing benefits among early adopters, from small physician office laboratories to large reference laboratories. Use of CQI and Six Sigma has contributed to financial savings and decreased TAT, lean production has improved test quality and reduced errors, and FMEA has decreased time to report critical laboratory values.

^y The CLSI five tiers of quality are: (1) QC; (2) QA, including PT; (3) QMS; (4) quality cost management; and (5) TQM, known as CQI in health care.

^z International Organization for Standardization (ISO) has developed two standards for QMS: the more general ISO 9000 series and ISO 15189, which is focused on health care. CLSI guidelines HS1-A2 and GP26-A3 facilitate the implementation of these standards.

- The great bulk of effort on formal performance measurement and improvement has been devoted substantially to the analytic phase, rather than the pre- and postanalytic phases. Public and private sector organizations have sponsored research and other initiatives to address some aspects of the deficit of information on pre- and postanalytic quality. However, the indicators used to date have not been uniformly defined or assessed for generalizability, and are subject to wide variation in their implementation.
- The emphasis of provisions under CLIA is largely structural, outlining policies, procedures, and documentation requirements as a condition for accreditation and certification. Aside from PT and corresponding false-negative and positive rates, process measures to assess the quality in the TTP remain relatively underdeveloped and are selected based on expert opinion rather than evidence-based outcomes and gaps in quality. Typically, research studies rely on high-level calculations of error rates (e.g., specimen rejection, specimen labeling, TAT). The evidence pertaining to the impact of laboratory testing on outcome measures— health outcomes, humanistic outcomes, and economic outcomes— remains sparse. A small body of research has examined such areas as the costs of the analytic phase of particular tests and the adverse consequences of incorrect test results.

Gaps, Needs, and Challenges:

- Stakeholders in laboratory medicine must address organizational obstacles to the implementation of QMS in order to achieve higher levels of quality, including resistance to culture change, lack of leadership and staff commitment to QMS, and insufficient funding of QMS activities.
- Most research on the adoption and results of laboratory quality to date has focused on the larger, hospital-based laboratories. Further research is needed to examine the specific challenges that smaller laboratories and POLs may confront when implementing process-related performance measurement and quality improvement programs.
- Substantial work is needed to support the selection, development and standardization of pre- and postanalytic process-related performance measures that are important to health care quality and patient-related outcomes, and satisfy minimum criteria such as those used by AHRQ's National Quality Measures Clearinghouse. Data collection, analysis, and reporting methods also need to be standardized.
- The evidence for the impact of laboratory medicine on patient outcomes, humanistic outcomes, and economic outcomes must be augmented. The lack of a substantial and evolving body of such evidence diminishes the ability to assess and demonstrate the value of laboratory medicine. Taking on this effort is essential in a health care market that increasingly demands evidence of value for adoption, use, and payment, especially for new health care technologies.

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CHAPTER VI

LABORATORY INFORMATION SYSTEMS

Laboratory information systems (LIS) have evolved over the past 30 years from simple systems designed to generate accurate reports to complete systems that can link laboratory data “end to end” across the TTP, including clinician-related pre- and postanalytic activities (e.g., test selection, interpretive consultation). Health information technology (HIT) and Web-based applications have enabled dramatic improvements in the ways in which laboratories communicate, provide services, educate their workforce and clients, market themselves to clients, and track clinical data and information.¹ Health care organizations have played a key role in advancing such communication by linking the LIS with hospital information systems, pharmacy database systems, etc.

As a strategic tool, the LIS should enhance quality and efficiency of health care professionals, allowing them to deliver high quality, cost-effective service.² In fact, several studies of urban and rural facilities have reported a direct association between the implementation of an LIS and improved financial performance.³⁻⁵

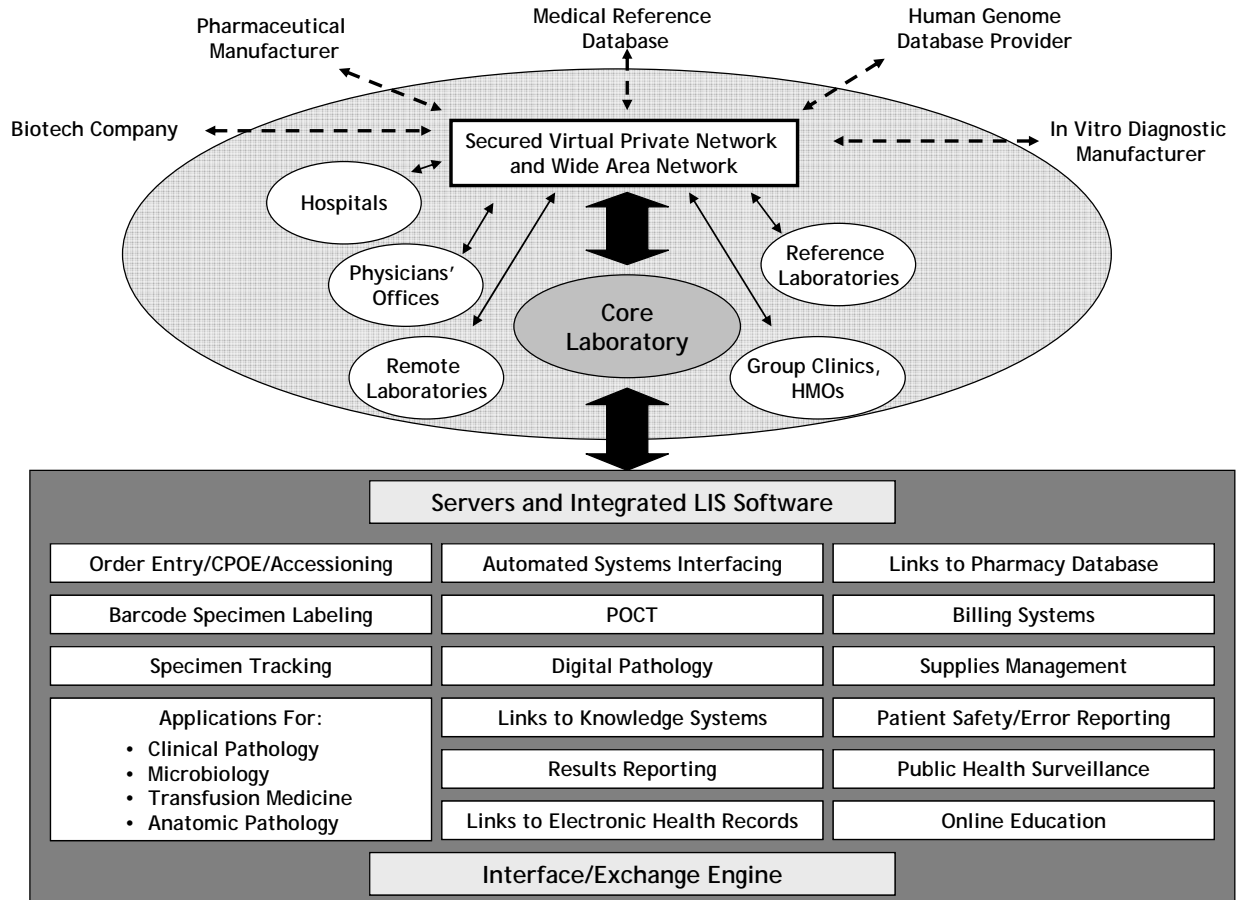
This chapter provides a brief overview of the basic structure of LISs in integrated delivery systems (IDS) and POLs. Particular attention was given to data management capabilities and clinical practice applications of interest to public and private sector stakeholders as they pursue comprehensive health information systems integration. In addition, the chapter discusses important informatics issues that continue to inhibit data exchange between applications both internal and external to clinical laboratories.

STRUCTURE OF LIS

Today, the LIS is a complex computer system of clinical and administrative applications programs with widely varying configurations in different types of laboratories (see Figure 6.1).⁶ An LIS may be a single, integrated software package running on one or more database systems. It also may be comprised of different modules (e.g., specimen accessioning, chemistry tests, and microbiology tests), often supplied by different vendors. Larger organizations may operate several LISs. For example, one LIS may be designated for general laboratory services, another for transfusion medicine, and a third for anatomic pathology. The traditional preference for interfaced,^a heterogeneous, best-of-breed systems appears to be shifting to integrated, single-source systems.⁷

^a An interface is a point of interconnection between a computer terminal and a network or between two networks.

Figure 6.1: Integrated Comprehensive Laboratory Information System



Adapted from: Cooper SD. The role of the laboratory information system in diagnostic services. In: Clinical diagnostic technology: the total testing process. Volume 1: the preanalytic phase. Ward-Cook KM, Lehmann CA, Schoeff LE, Williams RH, ed. Washington, DC: AACC Press, 2003.

Integrated Systems and Large Laboratories

An IDS is a group of health care service units (e.g., hospitals, outpatient clinics, ambulatory surgery centers, long-term care facilities, physicians’ offices, and hospital, POL and reference laboratories) that provide a spectrum of health care services across a geographic region.⁸ The LIS may operate across the network or group of networks in an IDS, although occasionally some operate in a closed or proprietary environment.

Within the IDS, a “core” laboratory serves as the primary testing site for the network. Smaller, rapid response laboratory systems operate locally where needed.⁹ While networking models vary by testing menus and location, the core laboratory usually performs most non-stat (non-urgent) and high complexity testing, including outpatient and outreach settings.⁸ In essence, the core laboratory functions as a reference laboratory serving both internal and external users.

The inter-laboratory connections are established by either a single LIS with multifacility function or multiple LISs that interface with the core laboratory.⁸ Multifacility systems typically rely on the computing hardware at one main data center and a common application interface standard such as health level 7 (HL7) for data exchange. Although all users can access the system, restrictions according to patient, provider, and facility identifier can be applied. Hardware standardization can increase efficiency in multifacility systems; however, this must be weighed against costs of replacing legacy systems. The multi-LIS model incorporates a central application interface engine in the IT architecture that routes and translates messages among the disparate systems based on predefined rules. Each site preserves its own security and access rules. While this option allows organizations to retain legacy systems, integration (via standardization and consolidation) requires major efforts to redefine certain database elements and standards across the different systems.

Linkages between hospital information systems and LISs are critically important to institutional systems and integrated delivery systems. The most “wired” interconnections are ordering of tests and reporting of results, claims and billing for tests, and links to the inpatient pharmacy database. The American Hospital Association (AHA) reported that, in 2007, 78% of hospitals had electronic reporting of laboratory results and 72% had laboratory test electronic order entry, either by the physician or within the laboratory.¹⁰ According to AHA, connectivity for laboratory reporting and ordering functions ranked on par with those for radiology (77% for reporting and 70% for ordering respectively), and ahead of pharmacy-related order entry (61%).

The VHA provides a real-world example of an integrated system, among the many in the public and private sector. In 1996, the VHA reorganized its 173 hospitals into 22 Veterans Integrated Service Networks (VISNs); each VISN is a regional health care system that provides a continuum of services to veterans residing in a specific geographic area.^{11, 12} Laboratory Electronic Data Interchange software consolidates electronic laboratory test ordering and results reporting throughout all VHA medical care facilities within and between VISNs.¹³ The VHA and Military Health System (i.e., TRICARE) are redesigning their networks to allow health information to be shared between the systems. Two of their demonstration projects specifically involve the LIS: the Bidirectional Health Information Exchange allows two-way exchange of health information, including laboratory results on shared patients in text format; and the Laboratory Data Sharing Interface application facilitates electronic transfer and sharing of laboratory orders and results.¹⁴

Modules

Most hospital and reference laboratory LISs are composed of multiple, separate clinical and administrative hardware and software modules (e.g., order entry, specimen tracking, report generation, accounts receivable, QC and QA, and automated instrument monitoring) that can operate either independently or be used as a system component. The main functions of hospital LISs are identified in Table 6.1. Currently, most LISs in reference laboratories do not link directly to clinical practice applications such as CPOE, POCT devices, EHRs, and pharmacy systems; however, data from their systems can be sent directly to providers electronically (e.g., results reporting) or be made available through regional health information organizations.^b

^b A regional health information organization (RHIO) is a group of organizations that are capable of electronic health care data exchange within a defined geographic region, usually via interoperable electronic health records. RHIOs are the building blocks of the National Health Information Network initiative proposed by the DHHS Office of the National Coordinator for Health Information Technology.

Table 6.1: Functions of a Laboratory Information System

LIS-related Application	Characteristics
<i>Preanalytic</i>	
Order entry/CPOE/accessioning	<ul style="list-style-type: none"> • Built-in functions for test ordering from standardized menus; may include automatic confirmation of medical necessity for performing the test • Clinicians may enter orders in hospital information system that will automatically transfer to the LIS, including appropriate laboratory location, time of day, priority status, or client • Algorithms may be used to assess appropriateness of test order in light of information contained in the LIS and in the patient’s medical record
Barcode specimen labeling	<ul style="list-style-type: none"> • Electronic identification of the health care provider, the patient, the specimen container, what specimen to collect, and the order in which the specimens were drawn
<i>Analytic</i>	
Specimen tracking	<ul style="list-style-type: none"> • Barcoded labels with unique identifiers for each specimen allow specimen to be tracked through the highly automated areas of the laboratory or from station to station during specimen examination • Tracking may be accomplished via scanning, either automatically or manually by the technician
Applications for clinical pathology, microbiology, transfusion medicine, and anatomic pathology	<ul style="list-style-type: none"> • Clinical pathology modules support specimen collection and tracking, order entry, rule-based decision making, results reporting, and interfacing with automated instruments <ul style="list-style-type: none"> ▪ Hematology modules allow for manual differential counts to be added, deleted, or masked to automated results when sent to the LIS and for the creation of histograms ▪ Immunology modules transmit data from enzyme-linked immunosorbent assay (ELISA) readers to LISs ▪ Toxicology modules automatically rerun positive results, generate complex random drug testing schedules for organ donors, and produce utilization reports to study testing trends • Microbiology modules allow for recording observations, additional test ordering, and creation of antibiograms (used by hospitals in the review of antibiotic usage) • Transfusion medicine modules automate transfusion services, including inventory, distribution of blood, quality control, and emergency release capabilities • Anatomic pathology modules provide access to patient clinical histories, links to clinical pathology department, correlation studies, and links gross and/or microscopic images to case worksheet and patient reports
Automated systems interfacing	<ul style="list-style-type: none"> • Allows laboratorians to manage and review large volumes of data and support QC requirements • QC functions track and review QC data from all workstations and perform statistical analyses to ensure that laboratory testing accuracy and precision are maintained at acceptable levels • Automatic functions for repeat testing on the same sample for either the same test, a different test, or different instrument, following an abnormal result or specific decision criteria • Enables manual results entry or automated result generation followed by automated results review and release (autoverification) • Blocking function prevents autorelease of results based on flags for abnormal results, delta check failure, panic value, improbable results, results failing user-defined criteria

LIS-related Application	Characteristics
POCT	<ul style="list-style-type: none"> • Supports POCT devices that link to the LIS via docking devices or infrared data transmission • Capable of receiving POCT data, creating and storing appropriate records, and generating final results reports
Digital pathology	<ul style="list-style-type: none"> • Digital photography, storage, cataloging, archiving, and dissemination of pathology images at the gross and microscopic levels • Supports electronic, multimedia communication of digital images between laboratories and clinicians, including telemedicine
Links to knowledgebase systems	<ul style="list-style-type: none"> • Links in LISs provide laboratorians access to knowledge bases containing clinical, genetic and molecular information (e.g., clinical definitions, gene ontology, protein structure and sequencing, mass spectrometry)
<i>Postanalytic</i>	
Results reporting	<ul style="list-style-type: none"> • Report formatting • Results reporting communications via fax, email, or Internet (usually through a virtual private network)
Links to EHR	<ul style="list-style-type: none"> • Links between LISs and EHRs being developed to allow laboratory results to be directly deposited into an EHR; eventually will include the ability to order tests directly from the EHR
Links to pharmacy database	<ul style="list-style-type: none"> • Supports linkages of pharmacy database systems to LISs for selection and management of medications and prevention of medication errors; links are generally from pharmacy system to LIS, not vice-versa
<i>Other</i>	
Billing systems	<ul style="list-style-type: none"> • Allows for generation of bills with minimal effort, automated coding of tests, generated from test orders • Supports accounts receivable to assist with management, receipt, collections, banking, and reporting
Supplies management	<ul style="list-style-type: none"> • Manages use, ordering, and inventory of supplies in the laboratory • Tracks lot number, quantity, and date received, opened, closed, and expired for reagents and other laboratory supplies
Patient safety and error reporting	<ul style="list-style-type: none"> • Alerts laboratorians when critical value has occurred and provides protocol to be followed, contact information for clinician, and log of time that message was delivered and name of person receiving it • Automation of quality assurance functions (e.g., documentation of abnormal results, TAT, list of corrected laboratory reports, comparison to standards set by CAP and other professional bodies) • Links between LISs and laboratory error databases in development to allow tracking of diagnostic errors made in the laboratory
Public health surveillance	<ul style="list-style-type: none"> • Surveillance and management reporting of infectious diseases and hospital acquired infections. • Communication functions with public health networks in the event of chemical or biological threats, emerging infectious diseases, and natural disasters
Online education	<ul style="list-style-type: none"> • Online laboratory manuals and handbooks, most often in Web-based form, to support knowledge and regulatory requirements

Sources: Adapted from Cooper 2003; Goh 2003; Li 2004; Grzybicki 2005; Asare 2000; Yuan 2005; Cimino 2004; Marchevsky 2002.

For hospitals and reference laboratories, certain more advanced modules such as digital pathology and telepathology already have been implemented. In addition, many hospitals are creating interconnections from LISs to clinical practice applications, such as CPOE, POCT devices, EHRs, and patient safety reporting systems. These advanced functions are vital components to the development of comprehensive information systems in hospital and ambulatory care settings.

Automated instruments for each subspecialty area (e.g., chemistry, hematology, microbiology) are linked to the LIS architecture. The combination of innovative automated equipment and IT has dramatically improved throughput, precision, convenience, and data handling.¹⁵ Linkages between modular systems and the LIS support QC and QA, consolidation of work and personnel, and more efficient integration and management of laboratory operations. Process control software allows the operator to monitor hardware, software, and work cell modules from one PC workstation.¹⁶

The LIS architecture is designed around workflow of analytic processes in order to enhance efficiency, decrease errors, and improve the overall quality of testing. Workflow analysis measures the impact of change in relation to laboratory costs and efficiencies.⁹ For each workstation involved in producing analytical test data, several factors are evaluated, including the age of analyzers, capital cost, throughput, service cost, supplies, and the labor associated with producing results. The data summary provides an estimate of the cost for each assay that is performed at each workstation. Computer simulation programs facilitate workflow analyses. The programs can imitate and capture dynamic system behavior, support workflow design, and evaluate alternative ways of improving efficiency and management.¹⁷ A good simulation model assists laboratory staff in determining the best configuration to reduce risks, costs, and turnaround time without disrupting the working system.

Interconnectivity

Each module or application can be used independently as a stand-alone unit or component, although some also have the capacity to import, export, imbed, or exchange data with other modules or applications. There are challenges to attaining optimum interconnectivity when the LIS modules are developed by different vendors using different data standards^c (e.g., data exchange, terminologies, document architectures, knowledge representation). As a result, many health care institutions must depend on middleware^d for connectivity and enhanced data management, especially for new, more complex laboratory testing technologies. Using “if-then” rule-based algorithms, newer middleware systems not only process data but offer flexibility in filtering, sorting, and displaying data.¹⁹ Development of middleware for data management stems from the need to resolve problems between instruments and the LIS (i.e., via workarounds) and to address the shortage of laboratorians available to manage and evaluate data.²⁰ Middleware serves the functions needed for today’s clinical laboratory that have not been met in the designs of

^c Data standards encompass methods, protocols, terminologies, and specifications for the collection, exchange, storage, and retrieval of information associated with health care applications, including EHRs, medications, radiological images, laboratory information, payment and reimbursement, medical devices and monitoring systems, and administrative processes.¹⁸

^d Middleware is software that facilitates communication between laboratory instruments and the LIS, or two applications, and management of workflow within a workstation or the system as a whole.¹⁹ Functions may include autoverification of results, addition of new orders to test files, insertion of comments, or take other actions for specific patients or physicians.²⁰

automated systems and interconnections with the LIS. A challenge arising from this third party approach is the integration of multiple, additional vendor applications and standards to the already complex pool, increasing opportunities for error.

Another important feature of LIS interconnectivity is the growing adoption of Web-based mechanisms to support electronic test ordering and results reporting executed from a hospital, physicians' office, reference laboratory, or other health care facility.²¹ Internet browsers running on personal computers allow direct data exchange between these facilities while portals provide gateways to the hospital LIS to access online ordering functions and retrieve results reports. Some Web-based applications allow results to be reported directly into a patient's EHR or a physician's practice management system.

Physician Office Laboratories

Increased regulatory requirements, testing costs, and coding complexity following the implementation of CLIA in 1992 accelerated adoption of certain LIS functions by some POLs.²² Similar to IDS, these systems help POLs comply with QC, PT, QA, and patient test management requirements. For QC, the LIS receives data from each instrument and evaluates whether values are within the control range. Along with PT data, the QC data are then stored for retrieval and review during inspections and for troubleshooting. LIS applications also are used to comply with CLIA patient test management requirements by automatically loading key data points (e.g., patient identifiers, lab name, address, age-specific normal ranges, units of measure, testing analyst, tests ordered).

For most POLs, use of other LIS applications is quite limited, because the majority of these laboratories perform waived tests and non-waived microscopy tests. Regarding interconnectivity, POLs that perform certain moderately complex chemistry and hematology tests (e.g., CBC) tend to structure analyzers as independent modules connected only to printers for report generation. If the POL has an electronic labeling function, it is usually connected to the office administrative application or the patient's EHR. Printed test results are added to a paper chart or manually entered into the EHR. Often, the EHR application includes an electronic ordering/reporting function that can link via the Internet to a larger reference laboratory with which the POL has an established business relationship. Generally, the need for broader access and more cost-effective networking solutions is boosting adoption of Web-based ordering and reporting capabilities in POLs.⁸

There is sizable cost involved in implementing and linking EHRs to other functions. While more physician offices are implementing them, it has become standard practice for reference laboratories to directly provide and/or finance basic electronic connectivity for ordering tests and reporting results. In doing so, however, external data exchange is limited to the "sponsoring" reference laboratory.²³ As this limitation inhibits compliance with open standards and development of health care data exchange, efforts are underway to require interoperability with other vendor systems. For example, MedPlus, Inc., an HIT subsidiary of Quest Diagnostics, has developed a program (now available) called "Universal Laboratory Orders and Results" that allows physicians' offices to electronically order and receive results and track patient laboratory and prescription data from both Quest laboratories and other hospital laboratories.²⁴

ADVANCED APPLICATIONS FOR COMPREHENSIVE SYSTEMS

Clinicians must have access to potentially pivotal patient information (e.g., laboratory results, medication list, and medical history) and to current scientific information (e.g., infectious diseases, medical evidence, guidelines) in order to provide high quality care. A comprehensive IT infrastructure is essential for:

- Managing the expanding volumes of clinical and administrative data generated from patient encounters
- Transforming clinical data into information that can be used to improve the safety, effectiveness, and efficiency of health care delivery²⁵

The infrastructure must ensure that laboratory and other data are accessible through efficient networks and clinical practice applications that link to the EHR.

Public and private sector initiatives to build the health information infrastructure have started with the ancillary services that generate the highest volume of data critical to patient care and safety – laboratory, pharmacy, and radiology. These services also tend to rely on sophisticated data management systems (e.g., LIS or pharmacy database) and innovative technologies (e.g., automated analyzer, robotic dispensing) for day-to-day operations. Links between the ancillary disciplines are necessary for accurate clinical diagnosis, treatment, and disease management. For example, links between clinical pathology and pharmacy data are needed for therapeutic drug monitoring, and links between anatomic pathology and radiology data are needed for diagnosis of cancer metastases and guidance of complex surgical procedures.

UNRESOLVED ISSUES RELATED TO ADVANCED APPLICATIONS

Automating Data Management

Effectively automating data management capabilities is an important factor in the evolution of the LIS and automation systems for clinical and anatomic pathology and requires informatics standardization, expanded computing power for new testing technologies, and other support for networked systems.

Automation of data management already has yielded several advantages to the clinical laboratory, including higher productivity and efficiency (e.g., higher test volume, fewer instruments), more streamlined workflows and easily reproducible processes, and decreased costs.²⁶

Current data management system designs have progressed from a hardware-based approach to a software-based approach that incorporates middleware and/or process control software. These applications generally automate such features as repeat testing, dilutions, reflex orders, and adjudication of instrument errors.^{e, 16, 27} For a middleware system to release results automatically, it must select from a range of actions based on various criteria and the desired scope of the

^e Repeat testing will be automated ultimately so that a specimen yielding a specific result can be returned to the system for additional testing using an alternative method or confirmatory testing on the same or different instrument. “Reflex testing” refers to additional testing performed automatically when a specific rule is applied to the result of the first test.

application which can differ by vendor, the type of test, and the nature of the patient population.²⁸ More sophisticated integrated systems incorporate knowledge-based process control software features and expert rules, such as algorithm testing, disease pattern checks, specimen integrity checks, clinical range checks, and delta checks.²⁹

Process control automates routine tasks and employs standards of practice to support the human operator. Although most common in large hospital and reference laboratories, process control software for automating data management is expected to increase sharply over the next several years. Process control features in development will facilitate the transportation, storage, and retrieval of laboratory specimens; physically identify and track specimens throughout the system; and support automated test cancellations and workload management. Next generation laboratory automation software will consolidate and integrate all aspects of laboratory, data, and instrument management from sample logistics to results management, archiving, and retrieval.³⁰ Successful integration of these process control data management features requires multidirectional, coordinated communication that links the LIS, preanalytic processing components, the specimen transportation system, analyzers, and the postanalytic archiving system.²⁸

Data Management for New Testing Technologies

The LIS must be flexible enough to handle the demands posed by new laboratory tests and technologies. In particular, the quantity of specimens involved in genetic, proteomic, and PGx testing pose significant challenges for LISs.³¹ The complete mapping of the human genome will continue to enable creation of new laboratory tests and LIS applications programs to support them.⁶

Greater use of genetic testing is increasing the need for LIS applications that support cytogenetic and molecular diagnostic testing. Examples of such applications include increased capacity for data storage, ability to detect genetic rearrangements and other abnormalities associated with malignant disease and hereditary genetic abnormalities, and ability to access patient records that contain personal gene databank and family tree information.³²⁻³⁴ Decision support, specimen tracking and automation of QA and QC documentation features also must accommodate the demands of genetic testing. In order to accomplish these goals, additional software applications and more sophisticated, high-speed computer processing capabilities are required of the LIS.³⁵

Extension of data management to genetic findings requires an LIS to standardize information and support genomics-based inference.³¹ Current medical vocabularies are insufficient to describe the findings generated by some new molecular tests.^{31, 36} Vocabularies such as the Clinical Bioinformatics Ontology have been designed for clinical molecular diagnostics and cytogenetics.³⁷ In order for LISs to handle the nature and volume of genomic tests, current discrepancies between how genetic mutations are described in the literature and how they are described in internet databases must be resolved.^{f, 36} Use of separate, specialized modules or systems in the laboratory that transmit summarized information to EHRs has been proposed as another means to allow LISs to meet the needs of genetic testing.³⁹

The upswing in genomic testing is speeding the integration of patient-specific genomic information into EHRs. Entering and formatting molecular diagnostic and cytogenetic laboratory

^f One example of an online database is RefSeq, a collection of genomic DNA, transcript, and protein products for major research organisms compiled by the National Center for Biotechnology Information.³⁸

findings into EHRs is necessary to support clinical decision-making and to automatically flag PGx-based risks.³¹

The volume and complexity of data generated from proteomic profiling, especially from high-throughput analyses and increased reliance on automation, demands that LISs be capable of storing large quantities of data.^{40, 41} In particular, LISs need to be able to search large internal and external databases containing information about proteins, which requires greater computing power than is currently available in these settings.^{40, 42}

PGx testing presents particularly difficult challenges to the LIS due to the potential enormity of its data requirements – molecular biology (e.g., sequences, structures, pathways), clinical medicine (e.g., medications, diseases, side effects) and pharmacology (e.g., pharmacokinetics and pharmacodynamics[§]).⁴⁵ Among other roles, PGx entails linking genetic information and clinical data in order to identify genotype-phenotype associations.

Patients also will need support when seeking, interpreting, and acting upon personal genetic-based data. The 2006 NACB draft guidelines on the application of PGx to the clinical laboratory recommends that laboratories develop educational resources to recipients of test results and that interpretative reports include a summary of the patient's metabolic status and its effect on the drug regimen being considered.⁴⁶

Computerized Physician Order Entry

Growing awareness of prescription errors and their associated costs provide some of the rationale for development and implementation of CPOE systems. These are online computer applications that allow physicians to order laboratory, pharmacy, and radiology services and therefore have the potential to prevent common medication ordering errors (e.g., selecting the wrong drug or dose, overlooking drug allergies).^{47, 48} Laboratory data are a vital component of CPOE systems and are often displayed for physician review prior to ordering.⁴⁹ CPOE systems must be able to exchange data with LISs using standardized communication protocols.^{47, 50}

CPOE adoption remains relatively low. A study reported in 2006 estimated that national adoption of CPOE is 15% in integrated delivery systems,^h 9% in stand-alone hospitals, and 1% in skilled nursing facilities and rehabilitation hospitals.⁵¹ Despite the use of interfacing standards such as HL7, messaging between the CPOE and LIS still requires customized programs and close collaboration between the laboratory and the team implementing the CPOE system.⁵² LISs face additional significant challenges in enabling CPOE, including how to provide real-time access to data stored in the LIS and how to ensure that the software-based rules governing the CPOE are appropriate and do not result in unacceptable rates of false positive and false negative alerts.⁵³

In 2000, the Ohio State University Health System implemented a CPOE system that linked bidirectionally with its LIS, automating the laboratory process from order entry to results reporting.⁵⁴ Compared to areas of the hospital in which CPOE had not been implemented,

[§] Pharmacokinetics refers to the activity of drugs in the body over a period of time, including the processes by which the body absorbs, distributes, localizes, and excretes drugs.⁴³ Pharmacodynamics refers to the reactions between drugs and living systems.⁴⁴

^h An integrated delivery system is an aggregation of acute care hospitals, rehabilitation hospitals, and ambulatory care practices.

laboratory TAT decreased by 25% and both work flow accuracy and efficiency increased. Extensive modifications made to their commercially available vendor-based CPOE system allowed the health system to interface with its other information systems and be tailored to physician needs. The ability to customize or adapt a CPOE system to an organization's needs is cited as a major consideration in a consensus statement on successful CPOE implementation published in 2003 by a group of 13 international CPOE experts.⁵⁵

The Leapfrog Group established an initiative to increase adoption of CPOE. Hospitals can meet Leapfrog's CPOE standard by assuring that physicians enter at least 75% of medication orders via a computer system with prescribing-error prevention software. In addition, the inpatient CPOE system must be able to alert physicians of at least 50% of common, serious prescribing errors, as well as allow physicians to electronically document a reason for overriding an interception prior to actually doing so.⁵⁶ Some vendors have offered CPOE systems as part of their information system products, making readily integrated CPOE systems more accessible to organizations that cannot develop their own systems.⁵⁰

Clinical Decision Support Systems

CDSSs rely on software algorithms designed to improve clinical decision making by matching characteristics of individual patients to a computerized knowledge base and generating patient-specific clinical options, recommendations and other support.⁵⁷ Such support may include alerts, reminders, order sets, reference information, and education.⁵⁸ Although currently available CDSSs require providers to enter patient data, forthcoming applications will automatically link to patient data held in EHRs and generate support features without duplicate entry.⁵⁹

Laboratory data are a key component of CDSSs. Currently, the most common laboratory-related feature of CDSSs is flagging abnormal test results.⁵⁹ Another feature in use among early adopters alerts physicians if they order additional, potentially redundant laboratory tests before results of previous tests can be obtained.⁶⁰ Eventually, CDSSs will include laboratory information that aids provider interpretation of medical symptoms, signs, and diagnoses. For example, systems developed at the Massachusetts General Hospital and Kaiser Permanente in Escondido, California, use symptoms, signs, laboratory data, and other clinical findings to produce a ranked differential diagnosis list.^{61, 62}

To supply laboratory data to a CDSS, an LIS must generate data interpretable by the decision support application. Laboratory data must be transparent enough to be understood, computationally unambiguous, and capable of being linked or adapted to multiple platforms.⁶³ Once laboratory data are transmitted to the CDSS, they may need to be reformatted to ensure their maximal clinical efficiency and efficacy.⁵² A major obstacle to the ability of a LIS to interact with and provide data to a CDSS is lack of interoperability between laboratory and clinical applications. The Clinical Context Object Workgroup (CCOW) of HL7 developed a standard to facilitate the integration of applications from many different systems at the point of use to give the clinical user the experience of interacting with a single system.^{i, 64} Widespread adoption of the

ⁱ The CCOW standard is based on context management, or the coordination and synchronization of applications so that they are mutually updated with the set of their common data objects (e.g., patients or medical encounters) that frame the user's interactions with applications.⁶⁴

CCOW standard would enable laboratories to seamlessly and efficiently exchange information with CDSS and other clinical tools.⁵²

To support CDSS, an LIS must have several complex capabilities. Decision making relies in part on rule-based systems or algorithms programmed into the LIS to automate processes such as reflex testing and alerts. While most modern LISs have rule-based capabilities sufficient for results autoverification, the capacity necessary to program a rule-based system for CDSS and the clinical and pharmacy data necessary to support these systems (e.g., QC and QA data, results of other laboratory tests, and historical test performance data) are not always available.⁵² Even once a rule-based system has been programmed; it requires regular updating to ensure that the knowledge base is current.

Point-of-Care Testing

Innovative sensor technologies, microprocessor-based analyzers, and disposable test cartridges have enabled the creation of small and portable testing devices that support minimally-invasive collection techniques, followed by rapid analysis and results presentation.¹ Examples of the many tests that can be conducted at the point of care include measurements of blood gases, blood count, glucose, drugs of abuse, and fecal occult blood.⁶⁵ More recently, technologies are enabling new and less-invasive POCT, such as minimally-invasive, laser-based skin perforators that collect interstitial fluid for measurements of glucose levels, and infrared sensors that measure glucose and other analytes through the skin.⁶⁶ Data captured in these devices can be downloaded via a docking station to a database that is linked to the laboratory or hospital information system, billing, and generation of summary data reports.⁶⁷

POCT devices in day-to-day patient care are expected to increase substantially in the near term, perhaps more so than any other laboratory-related technology.⁶⁷ However, one of the key unresolved issues in clinical settings is the lack of interoperability between POCT devices and the LIS.⁶⁵ The Connectivity Industry Consortium was formed in 1999 to develop a base-level interoperability standard for data exchange between POCT devices and EHRs and LISs.^{67, 68} The standard was transferred to CLSI and approved as *POCT1-A2: Point-of-Care Connectivity* (Second edition, 2006).^{j, 69, 70} It provides the framework for engineers to create medical devices, workstations, and interfaces that allow different types and brands of POCT systems to communicate with each other and LISs.⁷¹ CLSI developed additional guidelines for POCT device interoperability.^k In particular, *POCT4-A2: Point-of-Care In Vitro Diagnostic Testing* (2006) provides general definitions, procedures, and recommendations for POCT, including guidance on quality assurance, alternative QC, and specimen collection and identification.⁷² Two other guidelines target specific testing devices.^l

^j POCT4-A2 replaced its predecessor, AST2-A, published in 1995.

^k CLSI developed guidelines to provide users of POCT devices, including nonlaboratory personnel, with information and suggestions for good clinical testing practice and for producing reliable results regardless of where or by whom the test is performed.

^l *C30-A2: Point-of-Care Glucose Testing in Acute and Chronic Care Facilities* (2002) provides instructions and recommendations on the administration of a POCT blood glucose monitoring program, persons who perform the tests, selection of methods, reporting of results, and quality assurance.⁷³ *Guideline H49-A: Point-of-Care Monitoring of Anticoagulation Therapy*. (2004) provides information on how to proceed in the evaluation, implementation, and monitoring of heparin and warfarin therapy.⁷⁴

Technical issues (i.e., analytic performance, interconnectivity) are being addressed through international standards development initiatives; however, they have not yet been fully resolved. Many discrepancies between results from POCT devices and central laboratory values have been reported. For example, in a 2006 study comparing seven POCT glucose meters from four manufacturers to a central laboratory analyzer, differences greater than 10% were found 61% of the time for POCT *hyperglycemic* values, and differences of 20% or greater were found 57% of the time in the *hypoglycemic* range.⁷⁵ Some of these disagreements have been attributed to differences in testing methodologies between POCT and central laboratory testing.⁷⁶ Among these, POCT typically involves multiple instruments, each of which is operated by several people, as opposed to central laboratory testing, which generally involves one instrument that is operated by only a few people.⁷⁷

The lack of standardized hardware and software continues to challenge the integration of POCT devices with health information systems and applications. Until recently, vendors manufactured their respective devices with different data management features, data manager systems, and interface standards, resulting in high levels of redundancy in laboratory testing as well as significant additional costs.⁶⁷ As POCT becomes more common in inpatient and outpatient settings, the devices must be designed for interoperability with LISs and EHRs to support electronic storage, retrieval, and comparability of patient data for current care and future reference.

Electronic Medical and Health Records

Although often used interchangeably, electronic medical records (EMRs) and electronic health records (EHRs) are different. An EMR is a local (single provider) system installed in an organization to support secure, comprehensive, and electronic patient medical record information. An EHR is a *shared* information system that aggregates patient information from various systems and sites, including multiple patient EMRs, on a scale that is regional or broader. Because EHRs include EMR data, yet offer more extensive linkages outside the provider organization, U.S.-based initiatives have focused on building the health information infrastructure for the EHR.

Estimates of EMR and EHR adoption rates vary widely, often due to ambiguities in the definitions of EMRs and EHRs. The 2007 AHA survey on hospital use of IT reported that 11% of U.S. hospitals had fully implemented EHRs (mostly larger, urban, and teaching institutions).¹⁰ The Healthcare Information and Management Systems Society (HIMSS) has developed a database that maintains assessments of EMR implementation in approximately 4,000 hospitals using a scale of stage 0 (information systems for laboratory, pharmacy, and radiology not implemented) to stage 7 (the hospital has a paperless EMR environment).⁷⁸ December 2007 data indicate that nearly 39% of hospitals were in stage 2 and 28% had reached stage 3 or higher (see Table 6.2). However, the HIMSS definition of an EMR appears to fit the AHA definition of an EHR noted above.

EMRs and EHRs also are being implemented outside of hospital settings. A 2006 report and meta-analysis of quality-ranked studies sponsored by the Robert Wood Johnson Foundation estimated that 17-25% of physician offices, 13-16% of solo practitioners, and 9-57% of large

physician offices^m had implemented EHRs.⁷⁹ Despite relatively widespread support, three main barriers continue to inhibit widespread implementation:

- (1) Lack of adoption of common data standards for EHRs
- (2) Quick turnover of HIT companies
- (3) Cost of installing and converting to EHR systems⁸⁰

Table 6.2: EMR Adoption Model Trend Q3 2007

Stage of Adoption	Description of EMR Capabilities	Percent of U.S. Hospitals (N=4,381)
7	<ul style="list-style-type: none"> ▪ Medical record fully electronic ▪ CDO able to contribute to EHR as byproduct of EMR 	0.0%
6	<ul style="list-style-type: none"> ▪ Physician documentation (structured templates) ▪ Full CDSS (variance and compliance) ▪ Full Picture Archiving and Communications System (PACS) 	0.6%
5	<ul style="list-style-type: none"> ▪ Closed loop medication administration 	1.4%
4	<ul style="list-style-type: none"> ▪ CPOE ▪ CDSS (clinical protocols) 	2.2%
3	<ul style="list-style-type: none"> ▪ Clinical documentation (flow sheets) ▪ CDSS (error checking) ▪ PACS available outside radiology 	24.1%
2	<ul style="list-style-type: none"> ▪ Clinical data repository ▪ Controlled medical vocabulary ▪ CDSS inference engine ▪ May have document imaging 	39.1%
1	<ul style="list-style-type: none"> ▪ Ancillaries- laboratory, radiology, pharmacy 	15.0%
0	<ul style="list-style-type: none"> ▪ All three ancillaries not installed 	17.6%

Adapted from: HIMSS Analytics Databases (derived from the Dorenfest IHDS+ Database™). ©2007 HIMSS Analytics™

Because laboratory results are a major component of patient records (electronic or paper), interoperability between LISs and EHRs can reduce medical errors, increase appropriate and reduce unnecessary testing, and improve quality and efficiency of health care. Interoperability allows authorized clinicians (i.e., ordering and non-ordering) to electronically access laboratory results, view historical results, receive automatic alerts for critical values and abnormal results, and integrate laboratory data with other EHR-linked functions (e.g., CPOE, CDSS, disease management).^{81, 82}

Interoperability of EHRs and LISs is still in early stages of development, and most laboratory results cannot be directly integrated into an EHR.⁸³ Data transfer between systems has been hindered by incompatible programming platforms, components that prevent successful authentication and authorization of patients and providers, and security protocols. Existing LISs

^m Large physician office was defined as greater than 20 physicians by one study and as greater than 50 physicians in another study.

are devoted primarily to optimizing performance across internal system modules; data exchange with external systems is not a priority.⁸⁴ As part of a 2005 survey conducted by CAP, LIS vendors were asked about their products and the types of settings in which they were installed.⁸⁵ A majority of respondents indicated that a portion of their LIS installations were stand-alone and had not been integrated with other clinical applications (e.g., EHR).

The main barriers to EHR-LIS interoperability include technical complexity of developing data standards and costs. To date, initiatives to develop national standards for EHR-LIS interoperability have targeted results reporting for patient care and disease management. Several public and private sector initiativesⁿ are underway to address these constraints, including activities to develop data standards for EHR-LIS interoperability, including the following:

- The Health Information Technology Standards Panel (HITSP) is a multi-stakeholder coordinating body established in 2005 by the American National Standards Institute (ANSI). The EHR Interoperability Specifications are based on the DHHS Office of the National Coordinator for Health Information Technology Use Case for EHRs initiative.^o Designed as national standards, the specifications were developed using the data standards approved for the national HIT infrastructure.
- The EHR-Lab Interoperability and Connectivity Standards project (ELINCS), created by the California HealthCare Foundation (CHCF),^p developed a standard and detailed specifications for coding and formatting laboratory results messages delivered in real-time from the LIS to an EHR.⁸⁸ The standard can be used by commercial and hospital laboratories to send test results electronically and by developers/vendors in technical design of EHR systems. In 2006, CHCF funded pilot testing of ELINCS at five clinical sites, including three hospital-based laboratories and two national commercial laboratories.⁸⁹ Four of the five sites are currently operational,^q two of which have begun to extend ELINCS-based connectivity requirements to their data exchange partners (e.g., independent laboratories, other local hospital laboratories). Ownership of ELINCS is currently being transferred to HL7.

Digital Pathology

Recent advances in tissue labeling/processing techniques, imaging sensors, digital image processing, image analysis, and personal computers are transforming anatomic pathology and traditional microscopy. Digital microscopy is a form of digital pathology that integrates digital imaging and light microscopy to capture pathological images at the gross and microscopic levels.⁹⁰

ⁿ In October 2006, the federal government finalized new HIT safe harbor regulations for the Stark and anti-kickback regulations that allow for the provision of HIT below cost by a medical organization as long as the HIT increases patient safety and is interoperable with other information systems.⁸⁶

^o The Interoperability Specifications were developed from an assessment of the current practices in electronic laboratory results reporting, as well as from the EHR Use Case, which was created to describe interoperability between EHRs and laboratory systems from patient and provider perspectives.⁸⁴ The recommended standards put forth by HITSP were chosen to meet the requirements identified in the Use Case and to reflect current practice and future HIT needs and were chosen with the assumption that the standards will become more broadly used over the next several years.

^p CHCF has also led the development of CALINX, a standard to retrospectively communicate batch reporting of laboratory test results to data warehouses and disease registries to support population-level quality-improvement programs.⁸⁷ CALINX has been created to meet the specific needs of California.

^q The fifth site withdrew from the ELINCS pilot project after switching laboratory vendors.

The current rapid transition to digital media affords many advantages to pathologists, laboratory staff, and patients. The images may be electronically stored, replicated, cataloged, employed for educational purposes, transmitted for further interpretation (i.e., telepathology), analyzed for salient features (e.g., medical vision/image analysis), or used to support a wider digital pathology strategy. Digital images of pathologic slides also can support quality assurance by eliminating the need to cut and disseminate multiple sections for analysis. Following the substantial initial investment, digital technology costs less to operate than photographic prints. Memory cards, CD-ROMs, and other storage media that capture the images are inexpensive and can be reused. In addition, digital pathology shortens image production times.

The combination of automation technology with digital pathology has facilitated the development of automated cytology screening.^{91, 92} Cytology automation reduces the false-negative detection rate of manual, microscopic cytology examinations that rely solely on human evaluation. Computer-assisted systems can enhance human performance by identifying highly suspicious areas.

Digital technology is playing an important role in telepathology. The advent of telemedicine, i.e., the exchange of medical information electronically from one site to another to improve patients' health, has significantly changed the way pathologists compare and share diagnoses between institutions.⁹³ Traditionally, information shared includes stained and unstained slides, tissue blocks, wet tissue, and pathology reports.⁹⁴ Telepathology supports electronic multimedia communication between pathologists (and other authorized, trained laboratory staff) concerning primary diagnoses and second opinion consultations as well as consultations with other clinicians.⁹⁴ Information for telepathology consultations, including photographic and video images,^r is shared in three different ways: statically (information is stored and forwarded), dynamically (information is shared synchronously), and via a hybrid mode, which incorporates both static and dynamic sharing.

Educational institutions are incorporating digital pathology into their curricula as a user-friendly, interactive teaching method. Instructional databases include pathology slides scanned at high-magnification along with three-dimensional simulations of organs and links to other relevant literature, information, and diagnostic tools.⁹⁵ Some institutions also provide Web access to digital pathologic images.

Prominent issues in digital pathology pertain to image quality (e.g., optics and calibration of system components), standardization of image sizes, and Web-based connectivity.⁹⁰ High-power computation, large storage capacity, new image formats, and novel processing algorithms are needed to advance digital microscopy from multiple single-field images to whole-tissue-processing. High-content screening technology is necessary to meet genomic imaging requirements. Most pathology systems are currently designed as department-based applications; however, efficient and timely expansion of capacity for interpretive consultations requires broad implementation of Web-enabled, interactive telepathology.⁹⁶

^r In primary diagnosis telepathology, specimens at a referring site are diagnosed remotely by pathologists, and the pathologist at the remote site is solely responsible for the diagnosis. In second opinion telepathology, responsibility for the diagnosis belongs to the pathologist at the local site (known as the referring pathologist) and the remote pathologist (the consulting pathologist).

DATA STANDARDS FOR COMPREHENSIVE SYSTEMS

Lack of harmonized data standards is the greatest barrier to laboratories' ability to integrate data within the laboratory as well as to exchange data with external "trading" partners (e.g., hospital and ambulatory clinicians, other laboratories, pharmacy department, radiology department, public health entities, payers). Harmonization of data standards is at varying stages of completion and adoption for each application. However, further progress in building the health information infrastructure and integrating laboratory data with clinical practice applications cannot be realized unless the standards issues are resolved. Main components of data standardization are identified in Box 6.1.

Box 6.1: Components of Data Standardization

- Definition of data elements: determination of the data content to be collected and exchanged
- Data interchange formats: standard formats for electronically encoding the data elements. Interchange standards include sequencing and error handling, document architectures for structuring data elements, information models that define relationships among the data elements, user interface, and patient data links
- Terminologies: medical terms and concepts used to describe, classify, and code the data elements
- Knowledge representation: standard methods for electronically representing medical literature, clinical guidelines, and the like for decision support

Source: Institute of Medicine. Patient safety: achieving a new standard for care. Washington DC: National Academy Press, 2004.

The challenge of data standards for the broader health and laboratory information systems is not their absence, but their proliferation. The lack of uniform, common data standards creates great difficulty in establishing interoperability to transfer data easily and economically from one system or application to another. Although most standards are publicly available and developed by international standards organizations, some standards are proprietary and developed by private sector organizations. Traditionally, use of a standard in the U.S. has been voluntary and left to the discretion of the vendor or institution. As a result, an obstacle to achieving interoperability among information systems and applications has been the haphazard adoption of data standards across the board.⁹⁷ Historically, most laboratory-related systems and applications were designed to operate independently. Thus, lack of common data standards in laboratory medicine has inhibited information sharing between laboratories and health care providers.

Standards development organizations (e.g., CLSI), professional societies (e.g., HIMSS), and state and federal government agencies are collaborating to harmonize data standards specifications. Laboratory-specific technology integration initiatives include the following:

- The American Health Information Community (AHIC) was established in 2005 by the DHHS Office of the National Coordinator for Health Information Technology to provide the Secretary with recommendations for accelerating the development and adoption of HIT. To begin, the program will target standards harmonization and technology adoption in four areas: consumer empowerment, chronic care, biosurveillance, and electronic health records. This federal advisory committee is being converted to a public-private sector partnership. Several documents on laboratory-related integration can be found at:
<http://www.hhs.gov/healthit/community/background/>

- HITSP, discussed above, develops harmonized interoperability specifications, implementation guides, code sets, terminologies, integration profiles, and information policies. This panel provides input to the AHIC initiative. A summary of the recommended standards for interoperability can be found at:
http://www.hhs.gov/healthit/ahic/materials/02_07/ce/hitsp.doc
- The Laboratory Exchange meeting of public and private sector experts was convened by AHRQ in 2006 as part of the AHIC initiative to address challenges to data exchange between the LIS and EHR for test orders and results reporting. The meeting identified relevant business, financial, regulatory, data security, privacy and confidentiality, technical, and patient identification issues.⁹⁸ See:
http://healthit.ahrq.gov/portal/server.pt/gateway/PTARGS_0_217663_0_0_18/AHRQ_Lab_Meeting_Summary.pdf
- The HIMSS' Integrating the Healthcare Enterprise initiative was extended to clinical laboratories in 2003.⁹⁹ The international, private-sector initiative developed a technical framework that defines exchange partners, data exchange standards, and guidelines for integration of laboratory information and automation systems with the larger health care enterprise (i.e., hospital or IDS). See:
http://www.himss.org/ASP/topics_News_item.asp?cid=66712&tid=10

Efforts to harmonize standards and connectivity requirements through these initiatives have focused on data interchange formats and terminologies. Data interchange standards include encoding formats for data exchange as well as document architectures for structuring data elements, information models that define relationships among the data elements, user interface, and patient data links, all of which are needed to support high-performance interoperability. Because the HL7 standard for data interchange has been selected as the core standard for the health information infrastructure, the standard also is serving as the primary exchange and interface standard for LIS system-to-system, automation-to-LIS, and application-application connectivity. HL7 clinical document architecture is used for claims attachments to administrative transactions that use the ANSI American Standards Committee X12 standard for transmission. Other interchange standards address specific attributes or applications, such as the Unified Code for Units of Measure and Digital Imaging and Communications in Medicine standard.

Even though these standards are well integrated in stand-alone systems and first-phase data exchange, they are not sufficiently developed for next-level integration and interoperability for clinical practice applications. New means must be developed to represent data sets that are exchanged directly among EHRs or other end-user systems, consistent with CLIA requirements (e.g., where test was performed and methods used), and to accommodate ongoing changes and updates to laboratory reports in the EHR.⁹⁸ Also to be developed is the ability to associate laboratory test results with test orders, and patients with their providers in the EHR. The ELINCS project may offer a viable vehicle for specifying message standards to the rigorous degree necessary and to facilitate certification of conformance.

Important integration issues also include: record linkage and patient identification, data quality, data synchronization, business rules management, and real-time access.¹⁰⁰ Detailed descriptions and analyses of the informatics challenges of relating laboratory data to the EHR and other functions (e.g., biosurveillance) are provided in reports of HITSP, AHIC, and HIMSS cited above.

Controlled vocabularies facilitate data collection at the point of care, retrieval of relevant data, information, and knowledge, along with data reuse for multiple purposes such as automated surveillance and clinical decision support. The two vocabularies used in data interchange are the Logical Observation Identifiers Names and Codes (LOINC) and the Systematized Nomenclature of Medicine- Clinical Terms (SNOMED-CT). Unlike data interchange standards, many other code sets are used for different types of data. Examples include the Current Procedural Terminology® Fourth Edition and Healthcare Common Procedure Coding System.

Although LOINC is an appropriate terminology for laboratories and their coding, it is not readily applicable to health care providers.⁹⁸ Also, there is not a standard vocabulary for providers that maps unambiguously to LOINC. Wide variability in the way that common tests are named among the different terminologies and vendors (e.g., “serum sodium” versus “NA_S”), and codes for test batteries have not been fully developed for all local patterns that may be selected by providers. Another obstacle to the adoption of a common vocabulary is that most clinical data is stored in a natural language (free text) context that must be converted into an electronic format (structured, predetermined phrases and codes) prior to transmission.¹⁰⁰

Near-term LIS priorities for the laboratory medicine sector include achieving and implementing:

- Standardized ways of representing orders for laboratory tests
- Standardized means for reporting laboratory information in terms of both messaging format and test names
- Standardized approaches for correlating laboratory information with the correct patient
- Systematic, acceptable methods for maintaining privacy and confidentiality of laboratory data for public health surveillance and quality improvement purposes⁹⁸

CONCLUSIONS

LISs have evolved from systems to facilitate clinical laboratory workflow and generate results reports to complete systems capable of linking laboratory data through the entirety of the TTP, including clinician-related pre- and postanalytic activities. The extent of LIS adoption and capability varies; while IDS and large laboratories rely on LISs for many aspects of laboratory testing (e.g., test ordering, results reporting, links to the inpatient pharmacy database), POLs and smaller laboratories primarily use the LIS to facilitate compliance with QC, PT, QA, and patient test management requirements.

To improve quality and safety, manage the increasing volume of clinical and administrative information, and support emerging laboratory tests and clinical practice applications, LISs must increase computing power and conform to common data standards. All laboratories must develop Web-based connectivity to becoming fully integrated into the health information infrastructure.

- Successful integration of enhanced data management features requires multidirectional, coordinated communication that links the LIS, preanalytic processing components, the specimen transportation system, analyzers, and the postanalytic archiving system.

- The volume and complexity of data generated from genetic, proteomic, and pharmacogenetic testing, especially from high-throughput analyses and increased reliance on automation, requires that LISs be capable of storing and retrieving large quantities of data.
- Enabling CPOE, CDSS, and EHR applications with laboratory data in real-time requires continued development of rule-based algorithms capable of generating and integrating accurate alerts, reminders, order sets, results reports, and a list of differential diagnoses based on patient signs, symptoms, and characteristics.
- Digital pathology systems requires further advances in high-power computation, data storage capacity, image formatting, and processing algorithms to facilitate the shift from single-field images to whole-tissue-processing.
- Lack of harmonized data standards is the single greatest barrier to laboratories' ability to integrate data within the laboratory as well as exchange data with external "trading" partners. Further progress in building the health information infrastructure and the capabilities for integrating laboratory data more fully with clinical practice applications cannot be realized unless laboratories, health care organizations, vendors, and other stakeholders resolve data interchange and terminology standards issues.

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CHAPTER VII

FEDERAL REGULATORY OVERSIGHT OF LABORATORY MEDICINE

In the U.S. health care system, the purposes of regulation include one or more of: protect and promote personal and public health, advance personal and public health, and ensure that the public has access to sufficient, accurate information for using regulated products and services to improve their health. Regulation is designed to protect consumers by assuring certain levels of quality, such as acceptable performance, safety, and effectiveness of products and services; and to establish market conditions that will generate validated innovations for improving health, such as controlling elements of monopoly power, and minimizing fraud and abuse.^{1,2} The purpose of oversight by designated agencies and organizations is to enforce and otherwise achieve adherence to the rules and standards comprising regulation.

Three main elements of oversight are: information development and synthesis, standards setting, and compliance mechanisms.³ Information development and synthesis refers to the scientific studies, data collection, and reporting requirements for identifying and measuring potential benefits and harms of a product or service. Standards setting is a process for identifying and describing the attributes that a product or service should have in order to offer an acceptable mix of benefits and risks. Compliance mechanisms refer to the manner and extent to which standards are followed and enforced, varying from traditional “command and control” regulatory approaches to informal or voluntary approaches.

In its 2001 report, *Crossing the Quality Chasm*, the IOM characterized U.S. regulation of health care as a patchwork of laws, regulations, agencies, and accreditation processes through which each care delivery system must navigate at the federal, state, and local levels.⁴ The regulatory frameworks at the various levels are often inconsistent, contradictory, and duplicative, in part because of their often disparate origins, jurisdictions and evolution, as well as because their respective needs, priorities, and available resources are poorly articulated and inadequately coordinated. Moreover, current regulatory frameworks often lag behind changes in the health system, including those related to advances in scientific and medical knowledge and technological innovation. This chapter provides an overview of the federal regulatory oversight in laboratory medicine by CMS and FDA.

REGULATORY OVERSIGHT SYSTEMS

Regulatory oversight of the laboratory medicine sector is conducted at multiple levels by numerous governmental and non-governmental bodies. These include federal and state legislatures, federal and state regulatory agencies, professional and private sector organizations, and federal and state courts.

Legislative Oversight

The U.S. Congress establishes provisions for oversight through the passage of legislation that governs various aspects of laboratory medicine, including the Federal Food, Drug, and Cosmetic Act (FDCA) and CLIA. At the federal and state levels, legislatures can delegate authority to regulatory agencies to interpret, apply, and enforce the statutory standards.³ Federal and state

agencies providing oversight generally have clearly defined jurisdictions for which they may exercise regulatory powers and controls.

Federal Oversight

Several DHHS agencies share oversight responsibility for health care products and services at the federal level. In particular, CMS, FDA, and CDC have prominent oversight roles for clinical laboratories that generally complement one another. CMS is responsible for oversight of *clinical laboratories and their testing services* under CLIA. This includes implementation of the CLIA program and provisions that govern PT, QC, personnel requirements and training; laboratory inspections; enforcement of CLIA regulations; and approval of PT providers, accrediting organizations, and CLIA-exempt states.⁵ CMS' authority extends to oversight of tests developed "in-house" by a laboratory, i.e., laboratory-developed tests (LDTs), that may or may not have sought FDA approval. FDA is responsible for test categorization and for regulating diagnostic tests and certain software used in laboratory information systems under the provisions of the FDCA for medical devices. These tests are developed by manufacturers and regulated as *products*, e.g., test kits. CDC's responsibilities include conducting CLIA-related studies, convening CLIAAC, and providing scientific and technical support and consultation to CMS.

The DHHS OIG also has a role in oversight of clinical laboratories. The OIG conducts audits, investigations, inspections, and other evaluations to protect the integrity of DHHS programs, including FDA and CMS oversight, as well as the health and welfare of consumers and beneficiaries. OIG provides reports to the Secretary of DHHS and Congress on findings and recommendations for corrective action, as appropriate.

Other federal agencies regulating specific types of clinical laboratories include the DoD and the VHA. Laboratories in the DoD Military Health System are subject to CLIA requirements. However, a memorandum of understanding with DHHS permits MHS to operate independently following a successful review giving it "deemed status" for CLIA certification. In lieu of CLIA, separate legislative requirements govern laboratories in the VHA.

State Oversight

States can take a prominent regulatory role in laboratory medicine, although not all states uniformly do so. Currently, 26 states have some degree of statutory authority for oversight of clinical laboratories.³ A state may also apply to CMS for exempt status. If CMS approves, the state is recognized to be the primary regulatory authority of clinical laboratories within that state, and is determined to be exempt under CLIA. At this time, only two states, New York and Washington, are CLIA-exempt.

Private Sector Oversight

Other important sources of formal and informal regulatory oversight include professional and private sector organizations such as The Joint Commission and CAP. In a formal capacity, a federal oversight body may delegate regulatory oversight to selected organizations. Informally, many of these organizations set professional standards to which compliance is voluntary or a condition for accreditation.

Judicial Decisions

Legal remedies sought through state and, to a lesser degree, federal courts influence regulatory oversight. Tort actions brought to the courts can facilitate definition of standards, clarify interpretation of laws, and enforce compliance with regulations and standards of conduct among those that can be held accountable, including manufacturers, laboratories, health care providers, and other parties.

CLIA PROGRAM

Overview of Clinical Laboratory Improvement Amendments of 1988

Efforts to decrease laboratory error rates and improve the quality of laboratory testing led to the passage of the Medicare, Medicaid, and Clinical Laboratories Improvement Act of 1967 Programs (Public Law 90-174).^a To obtain a license under that law, laboratories were required to maintain records and equipment, perform QC, participate in PT, and set qualifications for laboratory directors and other supervisory personnel. However, the legislation did not define quality or set protocols to enforce performance standards, such as QC limits or PT criteria. Furthermore, laboratories receiving fewer than 100 specimens per year (mostly POLs) were exempt.^b Thus, as many as 25% of all tests performed on patient specimens were not subject to minimum quality standards.⁶

In the mid-1980s, the news media began to publicize the high incidence of laboratory errors in many of the nation's clinical laboratories, particularly reports of inaccurate test results from Pap smears.⁷ These media reports generated public and congressional concerns about the quality of clinical laboratory services in the U.S., prompting Congress to expand regulatory oversight of clinical laboratories.⁸ The resulting action was passage of CLIA 1988 (Public Law 100-578), which amended the 1967 law and revised the authority for the regulation of clinical laboratories conducting testing on "human specimens for health assessment or for the diagnosis, prevention or treatment of disease."⁹

The CLIA regulations, published on February 28, 1992, established explicit minimum standards for QA, QC, PT, record maintenance, certification, inspection, and personnel qualifications for all laboratories,^c including POLs.¹⁰ States and private organizations can have standards that are more expansive and/or more stringent than CLIA. Since its implementation, CLIA has served as the primary regulatory program governing the U.S. laboratory system. A revised final rule published on January 24, 2003, included a restructuring of QC and QA requirements in a quality systems framework.

^a The Medicare, Medicaid, and Clinical Laboratories Improvement Act of 1967 regulated laboratories engaged in interstate commerce by declaring that "no person may solicit or accept in interstate commerce, directly or indirectly, any specimen for laboratory examination or other laboratory procedures unless there is in effect a license for such laboratory issued by the Secretary under this section applicable to such procedures."

^b The 1967 law did not apply to laboratories whose operations were so small or infrequent as not to constitute a significant threat to the public health.

^c The regulations exclude three types of testing: forensic testing; research testing for which patient-specific results are not reported; and drug testing that is performed in laboratories certified and governed by the SAMHSA.

The requirements are organized according to test complexity and the level of risk associated with reporting erroneous results, rather than the type of laboratory in which testing is performed. Waived tests follow a different regulatory pathway than non-waived tests, e.g., moderate complexity tests, and high complexity tests. The regulatory requirements for each category are considered the minimum requirements necessary to ensure accuracy, reliability, and timeliness of laboratory test results.¹¹ Appendix C of the final rule, Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services, is used to determine compliance with the regulatory requirements of CLIA.¹²

Administration of CLIA

Chief authority for CLIA is delegated to the CMS, which conducts the program in conjunction with CDC and FDA under an interagency agreement. CMS has responsibility for all financial management and administrative operations of the program, including certification and fee collection, inspections, enforcement, accreditation and state exemption approvals, PT program approvals, and rulemaking. The CLIA program is funded entirely through user fees managed by CMS.

CDC conducts assessment studies; provides scientific and technical support and consultation to CMS in developing and revising technical standards, evaluating accreditation/exemption applications, reviewing PT programs, and developing technical information and educational materials; and manages the work of CLIAC.

FDA is responsible for laboratory test categorization, including test complexity and waiver determinations. The transfer of responsibility for test categorization from CDC to FDA allowed manufacturers of in vitro diagnostics (IVDs) to work primarily with one agency in pursuing requests to market their devices. Manufacturers now submit IVDs for premarket review (via the 510(k) clearance process or the pre-market approval (PMA) process, as appropriate) and requests for complexity categorizations solely to FDA.

In addition, professional and private sector organizations may apply to CMS for accreditation status and, if approved, are provided with the authority to accredit clinical laboratories, evaluate compliance with CLIA regulations, and educate laboratory staff to improve performance. Currently, six accreditation organizations have received such approval from CMS;^d approximately 25% of all laboratories receive accreditation through one of these organizations.¹⁴

^d Accreditation organizations may be granted “deemed status” for up to six years. Designees include: AOA, AABB, ASHI, CAP, COLA, and The Joint Commission.¹³

WAIVED TESTS

The original CLIA statute required laboratories performing one or more of a given set of nine types of tests or examinations (e.g., certain dipstick or tablet reagent urinalyses, fecal occult blood tests, ovulation tests) to obtain a CW from CMS^e and pay biennial fees. In a proposed rule published in 1995, DHHS clarified the criteria and process for applying for waived status.¹⁵ Under the proposed rule, waived status can be obtained if a test employs methods that are so simple and accurate as to render the likelihood of erroneous results by the user negligible or that are determined by the Secretary of DHHS to pose no unreasonable risk of harm to the patient if performed incorrectly.^{16,17} The FDA Modernization Act of 1997 contained provisions further amending these CLIA requirements, stating that a test will automatically be considered waived if FDA has approved it for home use.¹⁷

As a result of simplification of testing procedures and advances in instrumentation, the number of waived tests has increased dramatically. Tests that were once considered moderate complexity are being redesigned, and when they meet certain criteria for being simple and accurate, FDA may grant them waived status. These new waived tests are expected to make analysis easier, faster and more accessible to the public while maintaining reliability and accuracy.

Since implementation of CLIA, the proportion of laboratories performing only waived testing has increased from 20% to 58% of the more than 200,000 laboratories.¹⁸ From 1995 to 2005, the number of laboratories performing waived tests increased by more than 70% in clinical laboratories affiliated with non-exempt states and in POLs (see Table 7.1). Whereas there were approximately 200 waived tests associated with 9 analytes available in the U.S. in 1993, these numbers had increased dramatically by 2004 to more than 1,600 waived test systems that test for 76 analytes.¹⁸

**Table 7.1: Number of Facilities that hold Certificates of Waiver
1995 to 2005**

	1995	2000	2005	2007
Labs in non-exempt states	65,031	85,944	113,445	119,839
POLs	28,951	40,990	52,632	54,467

Source: CLIA update—June 2007. Centers for Medicare and Medicaid Services. CLIA database information, 2000. Centers for Medicare and Medicaid Services.

^e Still in the waived category, these tests include: (1) dipstick or tablet reagent urinalysis (nonautomated) for bilirubin, glucose, hemoglobin, ketone, leukocytes, nitrite, pH, protein, specific gravity, and urobilinogen; (2) fecal occult blood; (3) ovulation tests (visual color comparison tests for human luteinizing hormone); (4) urine pregnancy tests (visual color comparison tests); (5) erythrocyte sedimentation rate (nonautomated); (6) hemoglobin (copper sulfate, nonautomated); (7) blood glucose by glucose monitoring devices cleared by FDA specifically for home use; (8) spun microhematocrit; and (9) hemoglobin by single analyte instruments providing direct measurement and readout. See: 42 Code of Federal Regulations 493.15(c).

OUTSTANDING ISSUES IN WAIVED TESTING

Risk-benefit Tradeoffs

One of the factors contributing to the growth in waived testing is the increasing number of laboratories that are certified to perform only waived testing (Table 7.1).¹⁹ However, broad access to some tests in this category poses evolving risk-benefit tradeoffs to patients and other stakeholders.

An example that presents such tradeoffs is the OraQuick Rapid HIV-1 Antibody Test (OraQuick), a single-use qualitative immunoassay that detects antibodies to HIV-1 in a finger stick sample or whole blood. An IVD, OraQuick was originally approved via the PMA route by FDA in November 2002 as a moderate complexity test under CLIA. In January 2003, FDA granted CLIA waived status to OraQuick.²⁰ This made the test potentially available through many more health care providers and about five times as many clinical laboratories. In March 2004, FDA approved the test for detection of HIV-2 (a variant of HIV that is prevalent in parts of Africa but rarely found in the US) in whole blood, with continued waived status. Some in the public health community lauded the easier access to HIV testing and greater opportunity to reduce the number of individuals unaware of their HIV status. On the other hand, many in the laboratory community expressed strong reservations about the implications of waived status due to concerns about specimen adequacy, availability of counseling for HIV positive results when testing is conducted in a waived setting, and the reliability of the device. These concerns address whether specific waived tests really are so “accurate as to render the likelihood of erroneous results by the user negligible” and present “no unreasonable risk of harm.”^{21,22}

Oversight for Certificate of Waiver Facilities

Facilities that perform only waived testing are not subject to many of the CLIA regulations applied to those that perform non-waived testing, including QC, routine inspections, PT, and personnel qualifications and training. Although there is no routine oversight of these facilities, they are required to follow manufacturer’s instructions when performing testing and they must permit inspections by designated authorities as part of random compliance evaluations and complaint investigations.²³ Due to the large number of waived facilities and this corresponding lack of oversight, the government became concerned about conditions that have the potential to contribute to errors and patient harm. Several studies were undertaken to determine the extent to which waived facilities were meeting their obligation to follow manufacturers’ instructions and complying with other federal regulations requiring safe work practices.

During 1999-2001, CMS conducted preliminary on-site surveys of a representative sample of CW sites in 10 states. The pilot surveys detected certain quality concerns that had the potential to result in medical errors. In 2001, the OIG published a report following its investigation of CLIA certification and enrollment processes, identifying quality deficiencies in approximately 50% of CW sites.²⁴

In response to these findings, CMS reported results of nationwide on-site surveys of 4,214 laboratory sites during 2002-2004. (Such surveys are ongoing.) POLs comprised the largest percentage (47%) of CW facilities surveyed, followed by skilled nursing facilities (14%).¹⁸ About 90% of facilities performed no more than 5 different waived tests, and another 9% performed no

more than 10 different tests.^f The CMS surveys indicated that the majority of CW sites were aware of and followed manufacturer instructions; however, lapses in quality were identified at certain sites. About 5% of sites were conducting tests with a degree of complexity that exceeded their CW CLIA certification, which may compromise the accuracy of these tests and patient safety.^g The most frequently performed non-waived tests (72%) were direct microscopic examinations (e.g., potassium hydroxide preparations, wet mounts, or urine sediment examinations), although several other types of non-waived tests also were reported. In addition to conducting these non-waived tests, the sites were found to be non-compliant with CLIA requirements for laboratories performing non-waived testing.

For those facilities who were conducting only waived testing, 12% were not using the most recent manufacturer's instructions and 21% did not routinely check the product's package insert or instructions for changes to the information.¹⁸ Relative to manufacturer's instructions, 21% of CW sites did not perform QC testing and 18% did not use the correct terminology or units of measure when reporting results. Table 7.2 summarizes the prevalence of quality-related deficiencies in waived facilities. Data from the CMS surveys are similar to the findings of CDC-funded studies conducted from 1999 to 2003 by the Laboratory Medicine Sentinel Monitoring Network.^h These findings indicate a need for greater oversight of waived facilities, more stringent enforcement of manufacturer's requirements, and training of testing personnel. CMS has taken several measures to support more frequent site visits to CLIA-waived laboratories in order to monitor compliance of CW sites. Follow-up studies that evaluate the effect of strengthened enforcement on quality and safety in testing have not yet been conducted.

CMS has data from follow-up visits to CW laboratories indicating that the initial educational visits by CLIA surveyors contributed to improvements in these laboratories performance of at least 70%. CMS plans to continue this program of annual educational visits to a sample of waived laboratories.²⁵

^f The most common waived tests performed were glucose, dipstick urinalysis, fecal occult blood, urine human chorionic gonadotropin (visual color comparison), and group A streptococcal antigen (direct test from throat swabs).

^g Conducting non-waived testing can be potentially hazardous to public health since these facilities do not have the same QC measures as those certified for non-waived tests.

^h Laboratory Medicine Sentinel Monitoring Network is a CDC network established through CDC Cooperative Agreements with the state health departments of Arkansas, New York, and Washington.

Table 7.2: Number and Percentage of Quality Deficiencies Related to Following Manufacturer's Instructions and Documentation in Certificate of Waiver Sites from CMS Surveyed Sites* 2002-2004

Quality Deficiencies	No. of sites	% of sites
Following manufacturer's instructions [‡]		
The site did not:		
Have current manufacturer's instructions	485	12
Routinely check new product insert for changes [§]	701	21
Based on manufacturer's instructions, the site did not:		
Perform quality control testing	866	21
Report test results with terminology or units described in package insert	744	18
Adhere to proper expiration dates	267	6
Perform required confirmatory tests	265	6
Perform function checks or calibration	195	5
Adhere to storage and handling instructions	135	3
Perform instrument maintenance	125	3
Use appropriate specimen for each test	81	2
Add required reagents in the prescribed order	24	1
Documentation [¶]		
The site did not:		
Document the name, lot number and expiration date for all tests performed [§]	1,493	45
Maintain a quality-control log [§]	1,151	35
Maintain a log of tests performed	1,318	31
Require test requisition (or patient chart) before performing a test [§]	304	9
Keep the test report in the patient's chart [§]	56	2
Check patient identification [§]	31	1

Source: Howerton D, Anderson N, Bosse D, et al. Good laboratory practices for waived testing sites: survey findings from testing sites holding a certification of waiver under the Clinical Laboratory Improvement Amendments of 1988 and recommendations for promoting quality testing. MMWR Recommendations and Reports 2005;54(RR-13):1-25.

[†] N= 4,214 sites

[‡] Required for waived testing under CLIA

[§] 2003-2004 data only (n=3,317)

[¶] Not required for waived testing under CLIA.

NON-WAIVED TESTS

Diagnostic tests categorized by FDA as moderate and/or high complexity are considered non-waived. Laboratories performing these tests must comply with the regulatory requirements specified in CLIA for non-waived testing. Regulatory requirements include, but are not limited to, QC and QA, participating in periodic PT, and meeting qualification requirements for personnel. FDA categorizes the level of test complexity using specific CLIA regulatory criteriaⁱ (see Box 7.1). Together, these requirements facilitate a laboratory's ability to ensure quality testing.

Box 7.1: Test Categorization

To categorize a test system, assay or examination, a grade of 1, 2 or 3 is assigned for each of seven criteria, and scores are totaled. A score of ≤ 12 indicates categorization of moderate complexity, and a score of ≥ 13 indicates high complexity. Criteria include: (1) knowledge needed to perform test; (2) training and experience required; (3) reagents and materials preparation; (4) characteristics of operational steps; (5) calibration, quality control and proficiency testing materials; (6) test system troubleshooting and equipment maintenance; and (7) degree of interpretation and judgment required.²⁶

A subset of the moderate complexity category, PPM tests are specific microscopy procedures performed by a physician, mid-level practitioner or dentist during the course of a patient's visit (e.g., direct wet mount preparations for presence or absence of bacteria). Under CLIA, separate certification requirements were developed for PPM.^j

State Exceptions

A few states and territories expressed interest in applying for exemption from CLIA, notably California, New York, Oregon, Puerto Rico, and Washington. Washington was the first state to have its clinical laboratory licensure program judged equivalent to CLIA and therefore was granted an exemption from the federal regulation.^k New York State holds an exemption for all of its laboratories, except POLs. Oregon received exemption status on June 13, 1996, but formally notified CMS of its decision not to renew its application. Oregon's exemption period ended December 31, 1999.²⁷ Puerto Rico's request for exemption was denied on October 28, 1996.

When a state is granted an exemption from CLIA, CMS may no longer charge a fee to the laboratories in the exempt state. However, CMS does assess the state for its share of costs associated with CLIA. The regulation indicates that exempt states must pay for costs incurred through federal oversight investigations and surveys, their share of general overhead costs, and costs associated with follow-up complaints.²⁸ The weight of this cost for California, estimated at \$2.4 million annually, was the reason the state withdrew its initial application for exemption (after meeting all requirements to be granted an exemption).²⁹

ⁱ In accordance with CLIA, CDC categorized more than 25,000 test systems before the responsibility for categorization was transferred to FDA in 2000.

^j Tests in the PPM category include: (1) all direct wet mount preparations for the presence or absence of bacteria, fungi, parasites and human cellular elements; (2) all potassium hydroxide preparations; (3) pinworm examinations; (4) fern tests; (5) post-coital direct, qualitative examinations of vaginal or cervical mucous; (6) urine sediment examinations; (7) nasal smears for granulocytes; (8) fecal leukocyte examinations; (9) qualitative semen analysis (limited to appearance of sperm and detection of motility).¹⁶

^k Washington State Department of Health. Office of Laboratory Quality Assurance.

CLIA Standards

The CLIA technical requirements were designed to establish quality standards for clinical laboratory testing through the assurance of accuracy, reliability, and timeliness of patient test results, regardless of where the test was performed.³⁰ As noted above, the 2003 final rule reorganized the technical standards for laboratories performing non-waived testing to reflect the flow of a patient specimen through the laboratory (i.e., from receipt of the specimen with the test request through test performance and test result reporting). However, the core technical standards related to analytic phase QA and QC remain intact, including PT.¹ Although CLIA always required monitoring of all phases of testing, the reorganization more clearly aligns the regulations toward a comprehensive QMS-based approach. Laboratories must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess and, when indicated, correct problems identified in the preanalytic and postanalytic phases.³²

Data are limited regarding the impact of preanalytic and postanalytic QA. The next section provides a brief description of unresolved issues associated with QC and PT. Challenges concerning personnel qualifications and provisions for surveys and sanctions also are covered. Issues in regulatory oversight of genetic testing are discussed in a separate section. More extensive discussion on the new CLIA framework for systems-based approaches is provided in the Quality Systems and Performance Measurement chapter of this report. In a forthcoming report, CDC will publish recommendations of an expert workgroup for enhancing the effectiveness of PT.

OUTSTANDING ISSUES ASSOCIATED WITH CLIA STANDARDS

Methods for Analyzing PT Data

PT is an objective means of evaluating analytical test performance in a laboratory. It assesses whether compliance with CLIA has improved intra-laboratory quality.³³ All laboratories that perform non-waived testing are required to participate in PT. For most regulated analytes, each participating laboratory receives specimens three times a year from external, CLIA-approved PT providers.^{m,34} The laboratory tests these samples in the same manner that other tests are performed and reports the test results to their PT provider. The PT provider grades the results to determine their accuracy and compares them to peer groups or reference laboratory performance, i.e., inter-laboratory comparisons. PT is required for each specialty, subspecialty, analyte, or test listed in the regulations for which the laboratory is certified.

Failure to attain an overall testing event score of at least 80% is considered unsatisfactory performance for all specialties and subspecialties, except for gynecologic cytology (90%), ABO

¹ QA refers to the internal and external planned and systematic activities to monitor all components or characteristics that affect quality and customer satisfaction, including policies and procedures to ensure compliance with regulatory requirements. PT is an external QA mechanism. QC refers to the internal procedures and statistical analyses for day-to-day monitoring of analytic instruments and work processes, detecting problems, and implementing corrections prior to the delivery of products or services.³¹

^m Approved PT provider programs for 2007 include: Accutest, Inc., American Academy of Family Physicians, American Association of Bioanalysts, American Proficiency Institute, California Thoracic Society, COLA, CAP, Medical Laboratory Evaluation Program, New Jersey Department of Health and Senior Services, Commonwealth of Pennsylvania, Puerto Rico Proficiency Testing Service, Wisconsin State Laboratory of Hygiene, Maryland Department of Health and Mental Hygiene, ASCP, and New York State Department of Health.

group and D (Rho) typing (100%), and compatibility testing (100%). Unsatisfactory performance on two consecutive or two out of three testing events constitutes unacceptable performance for the laboratory.³⁵ A laboratory with an unacceptable performance rating must cease testing the failed analyte until it passes two consecutive “remedial” PT events. PT results are transmitted by the PT providers to a CMS database. According to the GAO, PT is the one available data source that can be used to uniformly compare laboratory quality across survey organizations.³⁶

Few studies have examined the long-term impact of PT on laboratory performance. A report published in 2007 examined PT performance in physician office, clinic, and small hospital laboratories during the ten-year period 1994-2004, using data from a PT provider, the American Proficiency Institute. The data showed failure rates for chemistry and hematology analytes declined significantly over the ten-year period. For example, failure rates for cholesterol testing dropped from 18.7% in 1994 to 3.2% and failure rates for glucose testing declined from 15.6% to 2.4%. Although failure rates for microbiology analytes also declined, they still exceeded 5% for certain tests in 2004, including positive genital/gonorrhea cultures, positive urine cultures, and Gram stains. Several limitations of the study were noted by investigators: the data were not stratified by type of laboratory and thus do not reflect the performance of laboratories that are newly-regulated under CLIA; PT focuses on the analytical phase of testing and cannot detect errors in the pre- and postanalytical phases; and the data reflect trends in a changing population of laboratories but not individual laboratory trends, making it difficult to determine if most laboratories improved or if poor performing laboratories ceased testing.³⁷ Studies by CDC and the State of California also have been instrumental in generating key assessments of PT success and failure rates in POL and non-POL settings.^{38, 39}

Similarly, the PT results do not necessarily indicate that a laboratory’s proficiency is sufficient to meet the needs of the clinician.³³ CMS would increase transparency of PT if it were to consider new ways to code certain tests for PT purposes, including disaggregation of tests within specialty areas. For example, as noted by the authors of the report referenced above on PT performance during 1994-2004, CMS aggregates all bacteriology tests (cultures, Gram stains, and susceptibility studies) under one code, which means that statistics depicting unsatisfactory performance in bacteriology (5.1% of laboratories) are somewhat misleading.³⁷ This is particularly the case in bacteriology, since methods of analysis can differ substantially, as some of these tests do not have analytes while others do. Instead, analyzing failure rates for individual tests would show more clearly those areas posing the greatest challenges in order to focus improvement activities.

Laboratories can interpret and use their PT results to improve their practices, along with their QC and QA data, whether or not grades are satisfactory.^{37, 40, 41} A recent study of detection and correction of systematic laboratory problems found that, although accredited laboratories generally perform well in PT, having the PT provider identify clusters of PT failures assists the laboratory in correcting the problems.⁴² Additional studies on the use of feedback from PT could facilitate further improvements in performance.

Cytology PT

CLIA mandates that all laboratorians involved in the testing of gynecologic cytology specimens participate annually in a CMS-approved PT program.^{n,o,43, 44} Cytology PT consists of 10 gynecologic cytology slides, which test-takers must examine and diagnose within two hours. Of the 12,831 individuals who took the initial test in 2005, 93% of cytotechnologists passed the exam, 67% of pathologists working without cytotechnologist passed, and 90% working with cytotechnologists passed.^{p,46}

Concerns have been raised about the structure of cytology PT programs. CLIA requires unanimous agreement among at least three anatomic pathologists in order for a slide to be included in a cytology PT program.⁴⁷ However, the regulations do not require that the slides be subject to the rigorous review usually undertaken during field validation studies. Some organizations^q have found that slides selected by expert pathologists as good examples of cytodiagnostic abnormalities ultimately fail field validation. A 2005 study of the CAP's Interlaboratory Comparison Program in Cervicovaginal Cytology reported that, of more than 10,000 conventional smears and ThinPrep cases selected by an expert panel of 3 cytopathologists, 19% of conventional smears and 15% of ThinPrep specimens failed field validation.⁴⁸

It is not apparent whether cytology PT programs lead to improvement in the quality of Pap testing. A 1999 study compared accuracy of diagnosis of Pap smear slides from 40,245 women examined by 81 cytology screeners with the PT scores received by the same screeners.⁴⁹ Correlation between the accuracy of diagnosis of the Pap smear slides and PT results led the researchers to conclude that performance on a 10-slide test gives only some indication of the true performance of screeners. A study published in 2000 found a low correlation between cytology PT and actual work performance. Researchers concluded that cytology PT should be considered just one measure of performance and should be evaluated in conjunction with other quality assessment monitors, such as re-screening studies, discrepancy rates, and workload patterns.⁵⁰

Several efforts could alter the structure of cytology PT. CLIA convened a workgroup to consider changes to the regulations in several areas: participation in educational programs, use of new technology (virtual media), testing frequency, number of challenges, categories of challenges, number of challenges per category, grading scheme, validation, test site, retesting, and confidentiality.⁵¹ CMS has been developing a Notice of Proposed Rulemaking based on the CLIA's recommendations. In 2006, the Cytology Proficiency Improvement Act was introduced in the Senate and the House (H.R. 6133, S. 4056), which would have amended CLIA to require all individuals involved in screening and interpreting cytological preparations to participate in annual continuing medical education programs in gynecologic cytology, rather

ⁿ Laboratories performing only nongynecologic cytology are not required to enroll in PT programs.

^o Three organizations are currently approved by CMS to conduct cytology PT: CAP, the State of Maryland Cytology PT Program, and ASCP.

^p Individuals have up to four opportunities to receive a passing score. After not passing on the fourth opportunity, they must cease examining Pap smears and must obtain at least 35 hours of continuing education in diagnostic cytology.⁴⁵

^q Slides that are donated to CAP's Interlaboratory Comparison Program in Cervicovaginal Cytology are reviewed by a panel of three expert cytopathologists; slides that are determined to be good examples of a single cytodiagnostic entity enter the PT program, after which they undergo a field validation process in order to designate each slide as "graded," a designation that marks that slide as being regularly and reliably identified by CAP cytology PT participants.⁴⁸

than in PT programs.^{52, 53} The bill, never enacted into law, was re-introduced in the House in 2007 (H.R. 1237).⁵⁴

Guidance on QC protocols, particularly for innovative testing technologies

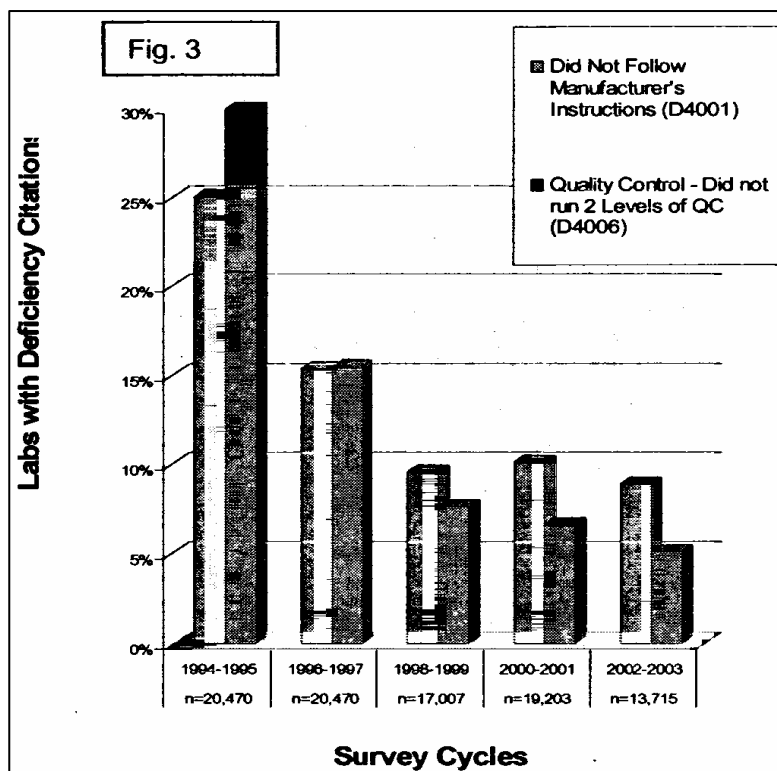
QC is designed to ensure that instruments perform as expected by controlling factors that affect test quality during the analytic phase, including technical and methodological variables, environment, and personnel performance.^r Generally, laboratories are required to run at least two levels of control per day, but the CLIA final rule considered technological changes in altering the frequency of QC testing in certain specialty and subspecialty areas of testing.⁵⁶ The CLIA interpretative guidelines provide laboratories with the flexibility to determine control procedures that are equivalent^s to the traditional QC frequency of two levels of control per day, i.e., “equivalent QC.”¹² The decision whether to implement equivalent QC is the responsibility of laboratory directors, not manufacturers or regulators, but can occur only if all of the laboratory’s quality systems are functioning properly.

Implementation of the CLIA requirements has resulted in significant decreases in the number of QC deficiencies (see Figure 7.1). A study of the impact of QC implementation in enzyme immunoassay testing for HIV-1 antibodies found that laboratories not using QC were at increased risk of systematic error, but adhering to CLIA requirements for QC was more protective against error.⁵⁷ However, several factors indicate a need for greater guidance in the area of QC, including the emergence of increasingly complex, innovative testing technologies (e.g., genomics, proteomics, PGx) and the need for immediate detection of errors and monitoring of ongoing test performance through QC protocols. Specifically, additional QC guidance is needed in light of the diversity of technology used to perform genetic and molecular-based tests, the rate at which this technology evolves, regional differences in the tests that are offered and the populations that are tested, and the lack of standardization of laboratory-developed genetic tests.⁵⁸ Given these factors, CLIA could fall short in assuring quality in laboratory testing in the future. CMS is working with the genetics community to develop specific guidance for laboratories to address these QC needs.

^r Under CLIA, laboratories also must implement and monitor quality systems for the pre- and postanalytic phases, thereby emphasizing the role of QA throughout the entire testing process.⁵⁵

^s The interpretive guidelines allow a laboratory to analyze two external controls per day for 10, 30, or 60 consecutive days to evaluate equivalent QC. If the comparison of internal and external controls is acceptable during this full testing period, the laboratory may adopt equivalent QC and increase the interval for analyzing external controls to every 7 or 30 days, depending on the equivalent QC option selected.

Figure 7.1: Percent of Labs with Major Quality Control Deficiencies



Source: Memorandum from Mark McClellan, CMS Administrator, to Leslie Aronovitz, GAO, May 17, 2006. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006.

During the phase-in, FDA was to establish a process to review and clear manufacturers' instructions for use in QC protocols.⁵⁶ Once approved, laboratories would follow manufacturers' instructions for QC rather than develop their own QC protocols.⁵⁹ The expected date for phasing-in this QC requirement was extended four times (December 6, 1994, May 12, 1997, October 14, 1998, and December 29, 2000) to allow completion of the phase-in period. In the final rule, laboratories^t retained responsibility for establishing and adhering to written QC procedures for monitoring and evaluating the quality of the analytical testing process for each method of testing.⁵⁶

Another concern is use of the interpretive guidelines in deciding whether to implement equivalent QC. CLIA states that the laboratory director must consider the laboratory's clinical and legal responsibility for providing accurate and reliable patient test results versus the potential cost savings of reducing the QC testing frequency.⁵⁶ Laboratory directors are likely to be aware of such tradeoffs in fulfilling their responsibilities; however, the lack of a framework for implementing QC for the wide variety of test systems may create inconsistencies in implementing QC.²³ Factors that contribute to these inconsistencies may include the lack of adequate risk management information from manufacturers, the different types and levels of QC required by each device and method, and the unique considerations of individual laboratories (e.g., personnel).⁶⁰

^t Although not part of the QC requirements, laboratories with unmodified FDA-cleared systems must include accuracy, precision, reportable range, and reference intervals in their procedures. For modified, non-FDA-cleared systems, analytical sensitivity, analytical specificity, and interference must be addressed. Validation studies must be provided for new methods.²³

To address these concerns, CLSI is working on the development of evaluation protocols that will outline principles for validation and provide laboratories with scientific guidance on the development of QC procedures for specific testing technologies and environments.⁶¹ In addition, CLIAAC members have reinforced the importance of laboratory directors' understanding of their responsibilities in implementing equivalent QC.⁶⁰

While flexibility in methods for QC (both general and equivalent) may be desirable, more comprehensive information is required than is currently produced by instruments.⁶² Technological advances have led to test systems that contain internal monitoring systems, but these newer types of control often monitor only certain elements of the test system.⁶³ For example, electronic controls may indicate the status of the test systems' electrical components, but may not alert the laboratory to trouble with environmental interactions. Similarly, systems may now include tests that cross specialty areas, making standardized QC impractical.

In some instances, the need to revise QC requirements was accomplished through stakeholder collaboration. For example, the American Society for Microbiology (ASM) conducted two surveys to determine the rates of QC failures for 24 microbiology reagents. ASM shared the resulting data with DHHS and recommended that, for commercial reagents with a 98% or greater success rate, only new lots need to be tested.⁶⁴ This resulted in a change to the CLIA QC requirements for microbiology reagents, as published in the 2003 final rule. A CLSI workshop held in 2005 discussed potential approaches for future QC, convening representatives from the laboratory, industry and government. As a result of the workshop, a proposal to revise the CLIA QC requirements for laboratories, using the CLSI consensus process, was developed by stakeholders and accepted by CMS.

In the absence of amending CLIA, some ways in which the laboratory community can improve QC include the following:

- Select QC procedures commensurate with the quality required for the test and the precision and accuracy observed for the method.⁶⁵
- Encourage manufacturers to include in their instruction explanations of the components of internal monitoring systems.
- Encourage manufacturers that want to diverge from traditional QC practices to demonstrate performance characteristics (improved stability of methods, better QC technology, etc.) and include such data in their dossiers submitted to FDA.
- Eliminate confusion on proper QC use.⁶⁶
- Collect and share among laboratories data on specific test system performance.

Personnel Qualifications to Meet Technical Requirements of Advanced Testing Methods

CLIA specifies personnel requirements for experience, education, and training, along with detailed corresponding responsibilities, that must be met by laboratories performing PPM, moderate complexity testing, high complexity testing, or any combination of these tests. Laboratories performing only waived testing do not have specific personnel qualifications.⁶⁷ A

summary of the CLIA personnel requirements for high complexity testing is provided in Box 7.2. The categories and requirements for moderate complexity are different.

Box 7.2: Summary of CLIA Personnel Requirements for High Complexity Testing

- *Director.* A director in a laboratory performing high-complexity testing has essentially the same responsibilities as a moderate-complexity testing laboratory director, including the overall operation and administration of the laboratory. A director must hold a doctoral degree in medicine, osteopathy, or one of the sciences and have appropriate board certification or one to two years of laboratory training or experience directing or supervising high complexity testing. Directors are limited to overseeing five laboratories at one time.
- *Technical Supervisor.* A technical supervisor is responsible for the scientific and technical supervision of high-complexity testing in specialties or subspecialties in which they are trained or have experience. Other duties are similar to those indicated for the technical consultant in laboratories conducting moderate-complexity testing. The requirements for a technical supervisor vary depending on the specialty or subspecialty in which the laboratory conducts high-complexity testing. Doctoral-level degrees are required for some subspecialties, including cytology, histopathology, dermatopathology, ophthalmic pathology, oral pathology, histocompatibility, clinical cytogenetics, and immunohematology.
- *Clinical Consultant.* The clinical consultant provides consultations to the laboratory's clients in matters related to reporting and interpreting test results. The qualifications and duties are similar to those specified for laboratories performing moderate complexity testing.
- *General Supervisor.* Unlike moderate testing facilities, high-complexity laboratories also have at least one general supervisor who provides day-to-day supervision of testing personnel and reporting of test results at the discretion of the laboratory director and technical supervisor. In order to qualify as a general supervisor, an individual must have a doctoral, master's or bachelor's degree in medicine, osteopathy or one of the sciences and one year of applicable laboratory training or experience, or have an associate's degree and two years of training or experience in high complexity testing. Subspecialties in histopathology require board-certified pathologists for the role of general supervisor.
- *Testing personnel.* Responsibilities of testing personnel include specimen handling and processing, test analyses, and reporting and maintaining records of patient test results. In order to conduct testing without direct supervision, testing personnel in high complexity labs are expected to have at minimum the education and training equivalent to an associate degree in a laboratory science or medical laboratory technology.

Note: Personnel qualifications may vary with test complexity as well as with date and year an individual was hired into a laboratory position.

Source: Laboratory requirements. *Code of Federal Regulations*, Title 42, Section 493. Subpart M--personnel for non-waived testing.

Technologists/scientists and technicians

The matter of determining personnel requirements for clinical laboratories preceded CLIA and remains controversial today. Two prominent laboratory professional societies and their members, ASCLS and ASCP, are collaborating to resolve their differing views concerning appropriate personnel qualifications and nomenclature (e.g., medical technologist vs. clinical laboratory scientist, medical laboratory technician vs. clinical laboratory technician). (Refer to the Workforce chapter of this report for a more discussion of the personnel qualifications advocated by these organizations.)

CLIA prompted some convergence among the organizations on these issues. The CLIA rule outlined minimum qualifications needed for individuals to work in a laboratory and offered pathways for an individual to perform high- and moderate-complexity testing. Rather than recognizing the titles of medical technologist or clinical laboratory scientist as approved testing

personnel, CLIA relied instead on education and training experience of personnel. Phase-ins permitted some individuals to continue their testing responsibilities until they could achieve additional education and training, and grandfather clauses allowed individuals with certain qualifications to continue testing without additional education, training, or experience.⁶⁸ Testing personnel responsibilities were outlined based on the complexity level of the tests.^{69, 70}

One concern for the professions was how the regulation would affect the National Labor Relations Board (NLRB) decision that technologists/scientists are considered professional employees. Nine amicus briefs were filed with the NLRB by laboratory professional organizations, including CAP, American Association for Clinical Chemistry, ASCP, and ASCLS, that highlighted the educational and training experience required for technologists/scientists. The briefs confirmed that, while automation allows technologists/scientists to work more efficiently, accurately, and productively, it does not replace the intellectual and analytical nature of their work. The NLRB agreed and upheld the educational and training requirements.⁷¹

Laboratory Directors

The matter of qualifications for laboratory directors prompted a different debate among laboratory organizations. Since laboratory directors are responsible for communicating laboratory data to physicians, including the interpretation for patient diagnosis and management, some believe that only a pathologist be qualified to fill this role, while others find it acceptable to permit doctoral scientists to oversee the laboratory. In its 2003 final rule, CLIA required that, after February 28, 2003, individuals with a doctoral degree in the chemical, physical, biological or clinical laboratory sciences seeking employment as a director of a laboratory performing high complexity testing must be certified by a DHHS-approved board.⁷² Physicians that are board certified in clinical and/or anatomic pathology continue to serve predominantly as laboratory directors, although some directors are certified by other boards.

Certification and Personnel Requirements

CLIA has provided impetus for change in the laboratory community. Laboratory organizations offering professional certification use CLIA as a minimum standard, which in some instances has meant increasing their personnel requirements. Other certifying bodies have used CLIA to build new career ladder opportunities, noting concern for the placement and retention of skilled personnel. For example, ASCLS is working toward development of advanced practice scientists, representing a doctoral degree in clinical laboratory science, to serve in consultant roles and manage patient laboratory data.⁷³ CLIA and its personnel provisions have prompted considerations to unite the ASCP Board of Registry and the NCA. In July 2006, the ASCLS Board of Directors, ASCP Board of Registry-Board of Governors, ASCP Board of Directors, NCA Board of Directors, and Association of Genetic Technologists Board of Directors reviewed and voted on a document outlining the rationale for such a union.⁷⁴

Personnel requirements for performing genetic testing are also at issue. A 2003 study of hospital-based, independent, and research-based biochemical genetic testing laboratories in the U.S. examined personnel qualifications using a mail survey of laboratory directors. Using survey responses, investigators assigned QA scores, which served as the main outcome measure of the study and were based on the standards defined by the American College of Medical Genetics Laboratory Practice Committee. The study found that, although all directors had doctoral

degrees, personnel qualifications varied. The mean QA score was 77%, with a range of 28-100%. Higher scores were associated with: laboratory director having a PhD degree versus MD degree; director board certification in biochemical genetics; research and hospital laboratory versus independent laboratory setting; and participation in a PT program. The investigators concluded that personnel qualifications and laboratory practice standards may need improvement to ensure quality in clinical biochemical genetic testing laboratories and appropriate use of test results.⁷⁵

Oversight Mechanisms Employed Through Surveys and Sanctions

Non-waived laboratories must permit biennial inspections to assess their compliance with the regulations as well as permit non-routine inspections to validate and investigate complaints. During the survey process, surveyors may require the laboratory to test samples and will observe testing, interview all levels of personnel, review copies of records, and tour all areas of the laboratory.⁷⁶ As noted above, laboratories with CWs are not subject to biennial inspections, but may be examined at any time to evaluate a complaint or assure compliance with CLIA.

CLIA provides CMS with the discretion to select the appropriate corrective action or sanction for identified laboratory deficiencies.⁷⁷ Enforcement mechanisms range from severe monetary penalties or onsite monitoring to cancelling a laboratory's approval for obtaining Medicare payments for its services or suspending or limiting a laboratory's CLIA certificate. Often, regulators take an educational approach and work collaboratively with laboratories to correct problems in lieu of imposing sanctions.

CMS also has implemented the Alternate Quality Assessment Survey (AQAS). The goal of this self-assessment survey tool was to streamline the CLIA inspection process and reward good performers. The AQAS form is consistent with the onsite survey process with a focus on QA. Laboratories with no deficiencies and satisfactory PT performance may use AQAS instead of having an inspection on their next two-year cycle. Approximately 5% of laboratories using the AQAS are inspected on-site to validate their self-assessment process.⁷⁸

The initial CLIA on-site surveys of laboratories in 1992 revealed quality problems in as many as 35% of laboratories; however, by 2004, fewer than 7% of 12,000 laboratories surveyed were considered to have quality problems. In 2004, CMS reported that it had proposed enforcement action in 6,084 cases since 1999, and implemented such action in 487 of them.⁷⁹ However, despite oversight mechanisms provided through CLIA requirements, laboratory quality problems in several states have raised questions about the adequacy of laboratory oversight.³⁶ For example, in 2003, the laboratory at Maryland General Hospital was among those identified with serious quality and management problems. Accredited by CAP, the laboratory was the subject of several inspections, arising from State inspections and complaints. A complaint by a laboratory employee alleged that the equipment used for HIV and hepatitis testing was not adequately maintained and that erroneous test results were possible. Oversight, management, and communication concerns in this case triggered congressional interest and a GAO investigative report on the status of CMS and survey organization oversight of clinical laboratories.^{79, 80}

In 2003, CMS regional offices followed suit and initiated a program to review and monitor state agency surveyors against 13 performance standards, including the training and qualifications of surveyors. However, the extent of serious quality problems at laboratories remained unclear because of incomplete data on condition-level deficiencies identified by state survey agencies

prior to 2004 and the lack of direct linkage between CLIA requirements and CLIA-equivalent requirements of some survey organizations.³⁶

The GAO's 2006 report to Congress concluded that oversight of clinical laboratory quality is inadequate to ensure that laboratories are meeting CLIA requirements, noting weaknesses in survey methods, complaint processes, and enforcement.³⁶ GAO stated that, aside from PT scores, there is lack of standardized means for measuring and reporting laboratory quality. Among its concerns, GAO suggested that the announcement of forthcoming inspections up to 12 weeks in advance may result in an unrealistic assessment of laboratory performance. The report observed that variability in reported survey deficiencies suggests that laboratories are not surveyed consistently. GAO also observed that CMS and survey organizations appear to stress education over regulation in the implementation of the 2003 QC requirements and PT for gynecologic cytology. Gaps in complaint processes compromise whistle-blower protection to those filing complaints about quality problems. GAO perceived that sanctions are not being used effectively as an enforcement tool to promote compliance even in laboratories with serious, consecutive, condition-level deficiencies. CLIA regulations require PT three times per year on analytes listed in Subpart I rather than the statutorily originally defined rate of four times per year. The report found that the length of time (2-4 years) allowed for implementation of new requirements is unnecessarily excessive and compromises quality. GAO noted that CMS was late in ensuring CLIA equivalence of exempt states' and accrediting organization inspection requirements, and that many of CMS' validation reviews lack independence and reviews skip some state survey agencies.

To address these issues, the GAO report provided 13 recommendations (see Box 7.3). CMS, CAP, COLA, and the Joint Commission were provided with an opportunity to comment on the report. CMS agreed with 11 of the 13 recommendations, the exceptions being the frequency of PT assessments and the extent of simultaneous accrediting organization validation reviews.³⁶ CMS also provided an alternative assessment of laboratory quality, disagreed with the GAO conclusion about the lengthy education phase-in for new CLIA requirements, and expressed concern about identifying and sanctioning laboratories with repeat condition-level deficiencies. CMS restated its intention to retain an educational approach to CLIA compliance, commitment to cite deficiencies appropriately when found, and provide additional training to state agency surveyors. CAP, COLA, and the Joint Commission agreed with some of the findings of the report, but disagreed with others.³⁶ Since the report's publication, CAP has implemented mandatory training for its surveyor team leaders, beginning on July 1, 2006.⁸¹ In response to GAO's recommendations, CMS has undertaken and completed certain actions and efforts intended to augment the CLIA program and strengthen oversight.

In 2006, CMS issued a guidance document, *Partners in Laboratory Oversight*, which identifies elements of an effective survey process that partner organizations are to incorporate into their respective survey protocols and suggests communication protocols for information sharing among partners. The guidance applies to CLIA activities among the CMS central and regional offices, state agencies (including those with licensure requirements), accreditation organizations, and CLIA-exempt states.⁸²

Box 7.3: Summary of GAO Recommendations to Improve Regulatory Oversight of Clinical Laboratories

Recommendation 1: To enable CMS to track the nature and extent of lab quality problems across survey organizations, the CMS Administrator should:

- Work with exempt-state programs and accrediting organizations to standardize their categorization and reporting of survey findings in a way that tracks to CLIA inspection requirements and allows for meaningful comparisons across organizations, such as the analysis of trends in the citation of condition-level deficiencies.

Recommendations 2-5: To ensure consistency in the oversight of labs by survey organizations, the CMS Administrator should:

- Ensure that the advance notice of upcoming surveys provided to physician office labs is consistent with CMS's policy for advance notice provided by state survey agencies.
- Ensure that regulation of labs is the primary goal of survey organizations and that education to improve lab quality does not preclude the identification and reporting of deficiencies that affect lab testing quality.
- Impose appropriate sanctions on labs with consecutive condition-level deficiencies in the same requirements.
- Require all survey organizations to develop, and require labs to prominently display, posters instructing lab workers on how to file anonymous complaints.

Recommendations 6-13: To improve oversight of labs and survey organizations, the CMS Administrator should:

- Consistent with CLIA, require quarterly proficiency testing, except when technical and scientific considerations suggest that less frequent testing is appropriate for particular examinations or procedures.
- Ensure that evaluations of exempt-state and accrediting organization inspection requirements take place prior to expiration of the period for which they are approved in order to ensure the continued equivalency of their requirements with CLIA's.
- Ensure that changes to the inspection requirements of exempt states and accrediting organizations be reviewed prior to implementation, as required by regulation, to ensure that individual changes do not affect the overall CLIA equivalency of each organization.
- Allow the CLIA program to utilize revenues generated by the program to hire sufficient staff to fulfill its statutory responsibilities.
- Ensure that federal surveyors validate a sufficient number of inspections conducted by each state survey agency to allow a reasonable estimate of their performance, including a minimum of one independent validation review for each state survey agency surveyor.
- Require that almost all validation reviews of each accrediting organization's surveys be an independent assessment of performance.
- Collect and routinely review standardized survey findings and other available information for all survey organizations to help ensure that CLIA requirements are being enforced and to monitor the performance of each organization.
- Establish an enforcement database to monitor actions taken by state survey agencies and regional offices on labs that lose their accreditation.

Source: Clinical Lab Quality: CMS and Survey Organization Oversight Should Be Strengthened. Government Accountability Office. June 2006.

GENETIC TESTING

Genetic testing is becoming an increasingly important component of health care delivery. In federal and state legislation, a genetic test is considered a DNA-based test, though the term is also used to refer to tests of gene products (proteins and metabolites), chromosomes, and acquired somatic cell mutations.⁸³ However, no single definition of a genetic test is universally accepted by all stakeholders.

Genetic tests can be used to “diagnose existing disease, to predict future risk of disease, to identify carriers of mutations that might cause disease in one’s offspring, or to identify particular traits in a fetus or embryo such as gender or human leukocyte antigen type.”⁸⁴ At present, genetic tests for at least 1,430 diseases are available for clinical use, and the number and availability of new tests continues to rise.⁸⁵ Given the life-altering influence that genetic test results can have, it is imperative that they be subject to adequate regulatory oversight.

PGx testing is a relatively new form of genetic testing. To date, only a few PGx tests are used to support decisions for selecting and dosing therapies.⁸⁶ Some early applications of PGx include *HER2/neu* testing to guide use of trastuzumab (Herceptin) for metastatic breast cancer, and thiopurine methyltransferase genotyping to manage the use of thiopurine drugs to treat acute lymphoblastic leukemia in children. Other PGx tests include *CYP2C9* and *VKORC1* testing to manage the use of warfarin for those at risk of harmful blood clots, the Roche Amplichip for *CYP450* mutations, and the *UGT1A1* test for irinotecan (Camptosar) sensitivity.

Currently, there are few laws and regulations that specifically address the complexity of genetic testing. At the federal level, oversight authority is provided through application of CLIA, FDA, and the Federal Policy for the Protection of Human Subjects. Specifically, while FDA has the regulatory authority for all tests, genetic tests developed as in-house (i.e., LDTs) are currently subject only to CLIA requirements, while tests developed by manufacturers are subject to FDA requirements. In addition, some state legislatures have introduced laws and regulations pertaining specifically to genetic testing. Reports by SACGHS and others have concluded that serious gaps in the regulatory framework for genetic testing could compromise patient and public health.⁸³

OUTSTANDING ISSUES IN GENETIC TESTING

Regulatory Oversight of Laboratory-Developed Genetic Testing

For the specialty of cytogenetics,^u CLIA provides specific requirements to address QC, PT, QA, analytical validity, and personnel.⁸³ However, the broader scope of genetic testing is subject only to CLIA’s general requirements for non-waived testing. Public and private sector stakeholders are working together to address outstanding concerns about the oversight of laboratory-developed genetic tests and personnel requirements of those performing genetic tests.

The CLIA Quality Systems final rule, published in 2003, restructured and updated certain requirements that are relevant to genetic testing, such as facility requirements for unidirectional workflow for molecular amplification procedures (§493.1101), quality system requirements for

^u Cytogenetics is the examination of chromosomes and the conditions caused by numerical and structural chromosomal abnormalities.

confidentiality of patient information (§493.1231), and QC procedures for PCR (493.1256).^{87, 88} These latest requirements do not include tailored QC, personnel, or PT requirements for molecular genetic, biochemical genetic, or PGx testing. Notwithstanding that genetic tests are high complexity tests, most genetic testing laboratories are not required by CLIA to perform formal PT, unless they are offering any one of the 83 regulated analytes. According to CLIA regulations, alternative performance assessment must be conducted for all other tests.

Consistent with earlier support by a National Institutes of Health-Department of Energy task force and CLIAC in 2000, SACGHS recommended that CMS develop regulations for genetic testing and that FDA review all genetic tests. In September 2006, CMS announced that it would not pursue a Notice of Proposed Rule Making for genetic testing. In August 2007, in response to a petition from the Genetics and Public Policy Center, CMS stated that supportive evidence does not justify rulemaking to establish a new genetics specialty under CLIA. Included in its rationale, CMS noted:

“Various tests that we would all regard as ‘genetic tests’ are in actuality dispersed throughout different operational sections of the laboratory and many are found in different existing CLIA specialties. Creation of a new genetic testing specialty would require not only greater precision in the current definitions, but would also require a teasing out of certain tests from some existing specialties, and cause some disruption to existing regulatory and payment structures.”

Instead, CMS stated that it would implement an action plan for enhanced oversight of genetic tests under the existing CLIA authority.⁸⁹ CMS is working with SACGHS, FDA, and other experts to address current gaps in oversight of laboratories that conduct genetic testing and to otherwise support or augment its action plan.⁹⁰ CMS has begun to implement its action plan, which includes:

- Training of surveyors in how to assess genetic testing laboratories’ compliance with regulatory obligations
- Collaboration with CDC to publish educational materials for genetic testing laboratories (e.g., *Morbidity and Mortality Weekly Report Recommendations and Reports*)
- Development of alternative PT mechanisms for genetic testing laboratories, such as inter-laboratory comparisons
- Collaboration with CDC and FDA on ongoing oversight activities^{91, 92}

CLIAC acknowledged CMS’ decision not to proceed with the rulemaking, but cited the need to examine the regulatory framework further in order to achieve enhanced oversight of genetic testing.⁹²

Some accreditation organizations also are addressing genetic issues related to laboratory-developed genetic tests. In 2007, CAP began an Internet-based registry service intended to connect genetic testing laboratories that perform low-volume genetic tests. When three laboratories are identified as testing for the same genetic disorder, CAP will facilitate an exchange of specimens for alternative assessment.

Enhancement of FDA's role in regulating laboratory-developed genetic testing

FDA has statutory authority to fully regulate all LDTs but has not done so because of resource constraints.³ With genetic tests of increasing complexity continuing to be marketed, often unaccompanied by direct evidence of clinical utility, there is a need to clarify or extend regulatory oversight of these tests.⁸⁴

In September 2006, FDA issued two draft guidance documents to address regulatory oversight of more complex laboratory-developed test devices that are used in genetic testing. One guidance document pertains to the marketing of in vitro diagnostic multivariate index assays (IVDMIA) and the other pertains to the marketing of analyte specific reagents (ASRs), which are the active ingredients used by clinical laboratories in developing LDTs.

In Vitro Diagnostic Multivariate Assays

Certain complex genetic and proteomic tests are IVDMIA test systems—tests that employ data from one or more in vitro assays, in some cases demographic data, and an algorithm that usually, but not always, runs on software to generate results for diagnosis and treatment. A great concern with these test systems is that the results cannot be independently derived and confirmed by another laboratory without access to proprietary information used in the development of the test. In addition, the results cannot be interpreted by well-trained health care practitioners without information from the developer of the test regarding its clinical performance and effectiveness. According to the 2006 draft guidance, FDA proposed to actively regulate these test systems as medical devices and classify them according to their intended use and level of control necessary to assure their safety and effectiveness, including requiring premarket review as class II or III devices, where applicable.⁹⁴

After receiving comments on the initial draft guidance for IVDMIA, FDA issued revised draft guidance for public comment in July 2007. The revisions clarified the definition of an IVDMIA and provided examples of tests that the agency does and does not recognize as IVDMIA. The agency noted that these clarifications did not alter the scope or intent of the definition of an IVDMIA that appeared in the initial draft guidance document.⁹⁵

FDA approved the first IVDMIA PGx test system, MammaPrint, in February 2007. Marketed in The Netherlands since 2005, MammaPrint is a gene expression profiling test for predicting whether an existing cancer will metastasize in women with early stage breast cancer.⁹⁶ As genetic testing and PGx, in particular, evolve, there will be ongoing need for guidance from CMS and FDA.

Analyte Specific Reagents

FDA regulates certain components of genetic tests that are developed and performed by laboratories, but that are not marketed as test kits. ASRs include antibodies, receptor proteins, nucleic acid sequences, and other biological or chemical reagents which, through specific binding or chemical reactions with substances in a specimen, are used to identify or quantify an individual chemical substance or ligand in biological specimens. Among other regulatory requirements, ASR manufacturers must list with FDA, follow quality system regulation, and restrict the sale of these reagents to high-complexity laboratories. FDA does not regulate how ASRs are used to create a new test. The great majority of genetic tests performed by laboratories are based on FDA-approved ASRs. FDA issued draft guidance in September 2006,

made final in September 2007, which clarifies the definition of ASRs and related regulatory requirements. Specifically, a single ASR that is (1) combined, or promoted for use, with another product such as other ASRs, general purpose reagents, controls, laboratory equipment, software, etc., or (2) promoted with specific analytical or clinical performance claims, instructions for use in a particular test, or instructions for validation of a particular test using the ASR, is considered by FDA to be a test system and, thus, is not exempt from premarket notification requirements.⁹⁷ The guidance addresses industry efforts to market increasingly complex combinations of ASR-based products (which might be considered test kits subject to premarket FDA review, rather than analytes) under the less demanding requirements of single ASRs. Indeed, there has been an increase in LDTs for simultaneous detection of multiple genetic variants. A related concern involves claims of multiple functions for a single ASR when selling it to a laboratory.^{98, 99}

Regulatory Oversight of Direct Access Testing for Genetic Tests

Some tests are being sold directly to consumers via Internet web sites and retail stores without the involvement of a health care provider in ordering the test or interpreting the results. The popularity of direct access testing is likely to increase given the rapid pace of genetic research availability of services via the Internet, and the growing interest of consumers in self-care.¹⁰⁰

When genetic tests are advertised and sold over the Internet or directly to consumers, significant clinical information may be missing or misleading, such as the clinical validity and utility of the test.³ For example, advertisements may de-emphasize the uncertainty of genetic test results, exaggerate the influence of a particular genetic polymorphism on health (e.g., likelihood of acquiring diabetes, heart disease, breast cancer, obesity), and exaggerate the positive influence the test can have on an individual's health. Reports of misleading information related to direct access genetic testing were published in a July 2006 GAO report.¹⁰¹ In that same month, the Federal Trade Commission issued a consumer alert on at-home genetic tests.

Consumers often lack the requisite knowledge to make informed decisions about whether to get genetic tests or how to interpret test results. Without the aid of a health care provider who can explain the advantages and disadvantages of being tested and implications of the results, and make sound recommendations on next steps, there is considerable potential for physical and emotional harm.

The wide variability in policies for direct access genetic testing among laboratories adds to the concerns. Although some laboratories require patients to provide the name of a physician to whom they may send the test results, others provide test results directly to the consumer. Similarly, although some laboratories have readily accessible genetic counselors to provide information and answer any questions that consumers may have about testing or their results, some laboratories do not.

Stakeholders have proposed ways to regulate advertising of and limit access to genetic testing. Careful regulation of advertisements could minimize misleading or exaggerated claims made by test manufacturers and providers, as well as limit the channels through which these advertisements are introduced. Regulating access to such tests would make it more difficult for consumers to obtain tests or results without authorization from a health care provider. This

measure would help prevent consumers from misinterpreting tests due to a lack of knowledge. Even so, efforts to impose more stringent restrictions on direct access for genetic testing may be challenged by consumers' desire for greater autonomy over their health care, including direct access to services and control of personal health information.³

Contrasting the FDA and CLIA Routes

FDA requirements for the 510(k) notification and PMA review processes for tests as medical devices and CLIA requirements for LDTs serve different purposes and rely on different data. In general, FDA emphasizes safety and efficacy of testing devices and CLIA emphasizes a quality testing process.

FDA has an agency-level responsibility for oversight via the 510(k) or PMA processes.^{102,103} This oversight involves considerations of analytical validity and clinical validity for tests to establish their safety and efficacy, particularly those subject to premarket review via the PMA route. However, resources are inadequate for review of analytical validity and clinical validity for many tests, and there is little or no agency oversight of clinical utility for nearly all tests. As noted above, due to resource constraints, FDA has not exercised its statutory authority to regulate all LDTs.

Among other aspects of quality described elsewhere in this report, laboratories must demonstrate analytical validity of tests through an initial inspection and subsequent biennial on site inspections. However, as standards of evidence for these inspections are determined by the individual laboratories, not CLIA, the quality of assessments of analytical validity for given tests can vary across laboratories. CLIA specifies (Subpart M – Personnel for Nonwaived Testing) that the laboratory director must “Ensure that ... [t]he test methodologies selected have the capability of providing the quality of results required for patient care.”⁶⁷ As such, CLIA vests considerable oversight responsibility in the individual laboratory directors. When a testing service is offered by a laboratory, its director is responsible for having determined that the testing service, as ordered by clinicians, is capable of providing the quality of results required for patient care. Further, the laboratory director is responsible for ensuring that the test is performed and reported properly and is subject to appropriate QC. LDTs can only be performed by the laboratories that develop those tests. In contrast to the national scope of FDA oversight, this is more decentralized, testing service-specific form of oversight.

Tests that are cleared or approved for market by FDA are available for use by any laboratories, and, like LDTs, are subject to PT and other CLIA oversight provisions. Most tests that are performed by laboratories are either cleared or approved by FDA or are LDTs. Some LDTs are based on ASRs that are regulated as medical devices by FDA. (As described above, recent FDA guidance has clarified that ASRs marketed in combination or alone, but with specific indications are, by definition, IVDs and subject to FDA regulatory oversight, accordingly.)⁹⁷ For the remaining LDTs that are not derived from these FDA-regulated products, the laboratory directors are still responsible for ensuring capability of providing the quality of results required for patient care. Certainly, many common LDTs that were not subject to FDA oversight have become standards of care over decades and have demonstrated, in practice, clinical validity and clinical utility.

Notwithstanding the means and extents of their respective oversight of analytical validity, clinical validity, and clinical utility, both the FDA and CLIA provisions are incomplete in their oversight of these attributes of tests. Whether for FDA-cleared or approved tests or LDTs, the

national capacity for establishing clinical validity and clinical utility, in particular, in field testing remains limited.

Market factors influence decisions to develop tests and can influence the regulatory route pursued for marketing a test or testing service. The likelihood of a manufacturer developing a test and collecting data sufficient to gain FDA clearance or approval is influenced by the size of the potential commercial market for that test. Pursuing an FDA pathway for a low-volume test may be economically prohibitive. Manufacturers may not find it commercially viable to pursue development and FDA review of tests for certain rare inheritable conditions or other “orphan” conditions affecting very small populations. Given the lower hurdles for reaching the market, laboratories may pursue such tests as LDTs and offer them as specialty or “niche” testing services. Manufacturers that choose to devote the necessary resources to generate data for gaining FDA approval to market a test may encounter competition from laboratories that develop and perform their own in-house version of the test. Compared to CLIA-regulated genetic testing, FDA-regulated tests generally are subject to greater scrutiny for clinical validity and, in some instances, clinical utility.

The current regulatory framework poses incentives for offering genetic tests as LDTs rather than marketing them via the 510(k) or PMA routes associated with FDA-regulated tests. While compliance with CLIA provides certain assurances of quality, launch of a genetic test (including, e.g., a PGx test) in the form of an LDT offers the advantage of more rapid access to market than launch of the test in the form of an IVD test kit or system that must be approved by FDA. Furthermore, even when a manufacturer has gained FDA approval for a genetic test, laboratories can develop their own version of the test and add it to their menu of CLIA-only regulated laboratory services. As noted above, depending on the benefit-risk tradeoffs of particular genetic tests to patients and clinicians, these tests may be more or less suitable for premarket clearance or approval by FDA.

TRANSFUSION-RELATED SERVICES

Transfusion-related services are critically important to the health and survival of millions of patients each year. More than 15 million units of blood were collected and more than 14 million units of blood were transfused in the U.S. in 2004, the most recent year for which data are available.¹⁰⁴

Since the early 1980s, the concept of blood banking has changed from being a laboratory discipline to the clinical and consultation specialty of transfusion medicine.¹⁰⁵ Concerns about transfusion-transmitted diseases contributed to this change, along with recognition of the success of transfusion-related laboratory services in addressing problems such as antibody identification and record keeping.

Protection of the blood supply is a multi-step process. Following collection, donated blood is tested in a clinical laboratory to detect the presence of pathogens and contaminants such as hepatitis B and C viruses, HIV, human T-lymphotropic virus,^v and syphilis.¹⁰⁸ If no pathogens or

^v Human T-lymphotropic virus can cause infections that can lead to leukemia or to a variety of neurological diseases.¹⁰⁷

contaminants are found and the specimen is approved, the blood undergoes further testing for ABO blood type, Rh factor, and unexpected red blood cell antibodies.

Clinical laboratories of large blood banking organizations are devoted exclusively to testing donated blood. The American Red Cross, which collects approximately 43% of all blood donated in the U.S., maintains five national testing laboratories and 32 blood manufacturing facilities.^{109,w} The laboratories test all blood collected by the American Red Cross, as well as some collected by other organizations. Laboratories providing transfusion-related services are subject to both CLIA and FDA oversight, and, as such must be certified by CMS and registered with FDA.

CLIA Requirements

CLIA regulations apply to the blood testing processes related to transfusion services. These laboratories must be certified and in compliance with the requirements for personnel, QC, QA, recordkeeping, and PT associated with performing high complexity testing and, when applicable, the specialty of immunohematology. For laboratories that are part of transfusion services but not involved in processing blood components, CLIA and FDA have a memorandum of understanding under which CMS assumes responsibility for regulatory oversight.¹¹⁰

CMS or CMS-approved accrediting agencies can assess compliance with CLIA regulations as well as with their own standards. Most transfusion service centers are accredited and surveyed by AABB. AABB currently accredits 221 laboratories and almost 1,600 organizations.¹¹¹ CAP inspects laboratories using its transfusion medicine checklist, providing on-site inspections on a biennial basis with facilities completing interim-self assessments during alternate years.¹¹² The Foundation for the Accreditation of Cellular Therapy runs a voluntary standard setting, inspection, and accreditation program for facilities involved in cellular therapy and cord blood banking.¹¹³ The Joint Commission also assesses transfusion services and donor centers within hospitals.¹¹⁴

AABB is not a CMS-approved PT provider, but administers PT for laboratories seeking accreditation as an immunohematology reference laboratory.¹¹¹ CAP offers two PT programs^x for blood testing laboratories, one for laboratories involved in transfusion medicine (J-survey) and one for automated transfusion medicine laboratories (JAT-survey), in which more than 4,500 laboratories currently participate.¹¹⁶ CLIA's PT requirements for laboratories performing transfusion related testing is more stringent than for most other specialties. A score of 100% is required for a satisfactory performance for ABO grouping, Rh D typing, and cross matching and 80% for antibody detection and antibody identification. (Eighty percent is a satisfactory PT score for most other specialties.)

FDA Requirements

FDA seeks to ensure that blood and blood products are safe for transfusion. FDA regulations apply to the components of blood product processing, including blood collection and testing, and

^w The American Red Cross' national testing laboratories are located in Charlotte, NC; Portland, OR; Detroit, MI; St. Louis, MO; and Philadelphia, PA.¹⁰⁹

^x The J-survey is mailed to subscribing participants three times each year and tests participants on determination of ABO group, Rh D type, antibody detection and identification, and cross-matching.¹¹⁵

mandate that blood testing laboratories implement QA and QC functions. Laboratories performing tests on donated blood must use only FDA-approved tests.¹¹⁷

Blood is regulated as a drug, as defined in section 201(g) of the FDCA, and a biological product, as defined in section 351(a) of the Public Health Service Act.¹¹⁸ FDA's Center for Biologics Evaluation and Research holds primary statutory authority to regulate and set standards for all aspects of blood banking, including collection procedures, blood components used for transfusion or manufacturing of pharmaceutical products (e.g., clotting factors), and products that ensure the safety of the blood supply (e.g., cell separation devices, blood collection containers, and HIV screening tests).^{119, 120} The Center for Biologics Evaluation and Research also has authority to conduct regular unannounced inspections of blood banking centers and investigate reports of blood-related errors, accidents, and adverse clinical events.

Title 21 of the Code of Federal Regulations (CFR) outlines the specific provisions to which laboratories and manufacturing facilities must comply, e.g., licensing requirements, QA procedures, product standards, and current good manufacturing practices. Each laboratory must designate an individual who is responsible for ensuring compliance with regulations by all personnel and who will serve as the facility's representative to FDA.¹²⁰ Each facility's QA operational framework must provide designated individual(s) with the authority to report serious infractions directly to FDA and, if applicable, stop production immediately.¹²¹

At a minimum, FDA conducts biennial inspections of blood testing laboratories and manufacturing facilities, usually unannounced, to assess compliance with the CFR. More frequent inspections may be undertaken if compliance problems are identified. Inspections are based on a multi-layered set of safeguards highlighted in Box 7.4.¹¹⁷ Advisory, administrative, and/or judicial enforcement mechanisms^y are available to FDA in the event that inspection findings demonstrate operational deficiencies and/or management is unwilling or unable to implement corrective actions in a timely fashion.

Box 7.4: Safeguards for Inspection of Blood Banking Laboratories

- Donor screening: donors are informed about potential risks and are required to answer questions about factors that may influence the safety of their blood
- Blood testing: each unit of donated blood is tested for infectious diseases
- Donor lists: blood establishments must keep a current list of deferred donors and must ensure that blood is not collected from anyone on that list
- Quarantine: donated blood is quarantined until it is tested and proven to be free of infectious agents
- Problems and deficiencies: blood centers must investigate manufacturing problems and correct all deficiencies; they must also notify FDA when product deviations occur in any distributed products¹⁰⁷

Source: Keeping blood transfusions safe: FDA's multi-layered protections for donated blood. Rockville: Food and Drug Administration, 2002.

Industry stakeholders perceive several regulatory constraints in the area of blood banking. Many of these issues are related to manufacturing (e.g., cellular therapies, plasma preparation) and tissue storage and are, therefore, outside the scope of this report. Those issues related directly

^y Mechanisms include warning letters, license revocation or suspension, seizure of products, injunction and prosecution.

with laboratory testing (e.g., recruitment of donors, health history questionnaire and emerging threats to blood supply) are discussed below.

OUTSTANDING ISSUES FOR TRANSFUSION-RELATED SERVICES

Simplification of Donor History Questionnaire

Physical assessment and a medical history interview are tools used to determine a donor's eligibility to donate blood and blood components.¹²² Since the first formal uniform donor screening questionnaire was developed in 1953, the number of questions and the amount of information that it captures as a part of donor screening has increased, reflecting advances in identifying risks of disease transmission.

In 2000, AABB organized a multi-organizational task force to address concerns related to the donor assessment process with the goal of reducing the complexity and improving comprehension of the questionnaire and supplementary education materials. The task force produced the Uniform Donor History Questionnaire (DHQ), a new set of documents that includes a full-length questionnaire (of 17 specific questions), user brochure, medication deferral list, and blood donor educational materials. While FDA does not mandate the use of a particular screening tool for donors to assess risk of communicable disease, it does recognize the DHQ as an effective donor screening tool through which licensed and unlicensed facilities can meet regulatory obligations.¹²³

An abbreviated DHQ (aDHQ) was developed as an alternative for a specific subset of repeat donors.¹²⁴ The aDHQ originally proposed by the AABB task force consolidated the 17 questions about medications and medical events on the full-length DHQ into one medical history capture question that asked donors whether they had any new medical problems, diagnoses, or treatments, including vaccination, since their last donation.¹²⁴ However, FDA expressed concern about the ability of one question to capture important information. The aDHQ was revised to include two medical questions that ask whether donors have had any new medical problems or diagnoses and whether they have had any new medical treatments since their last donation. However, unlike the full-length DHQ, FDA has not officially recognized the aDHQ.^{125,z} Additional work is needed to improve the ability of abbreviated forms to account for the medical history of donors.

Mechanisms to Handle Emerging Threats to Blood Supply

FDA's ability to handle emerging threats to the blood supply, such as new HIV variants, new hepatitis agents, Creutzfeldt-Jakob Disease, bacterial contamination of blood products, and others, has significant impact on the public health.¹²⁷ In many cases, blood collection organizations choose to implement specific screening tests prior to FDA issuing guidance. For example, FDA does not currently require blood collection agencies to test for West Nile Virus or Chagas' disease, two diseases that are increasingly prevalent in the U.S. However, the American Red Cross currently tests all of its blood for contamination with both of these diseases. This decision was based primarily on the recognition that blood collected by the organization in one part of the U.S may be shipped to another area for transfusion, rendering the geographic clustering of the

^z Licensed blood establishments that plan to implement a version of the DHQ materials that have not been officially FDA-recognized must submit a formal request to FDA for approval.¹²⁶

diseases less meaningful. According to some reports, approximately 70% of all blood centers in the U.S. are testing blood for Chagas' disease.¹²⁸

A 2006 IOM report on the future of drug safety provided recommendations to FDA related to protecting and improving the safety of the blood supply.¹²⁹ In response to IOM's recommendation that FDA strengthen the scientific base that supports their medical product safety team, and as a result of FDA's self assessments, FDA began working with CDC in 2006 to identify new threats to the blood supply and to develop, evaluate, and deploy modern technologies to address them.¹³⁰

CONCLUSIONS

CLIA 1988 has served as the primary regulatory program governing the U.S. laboratory system since its implementation in 1992. The final rule addressing quality systems and certain personnel qualifications was published in 2003. The CLIA program is administered as a tri-agency effort that involves CMS, which has primary oversight of the program, CDC and FDA.

The current CLIA regulatory framework for clinical laboratory testing, including its goal to ensure high standards of quality, promote access, and improve patient outcomes, is limited in certain important ways by its language and by the time frame required for development and amending relevant regulation. Rapid technological advances, demographic shifts, lower tolerance for error, and higher expectations for personal data security are challenging and, perhaps, outstripping certain aspects of the current regulatory framework for clinical laboratories. Population and epidemiological trends are increasing the incidence and prevalence of chronic diseases; broader screening benefits and coverage of prescription drugs for Medicare beneficiaries are contributing to the demand for rapid and patient accessible laboratory testing for screening, diagnosis, and therapeutic monitoring.

- CLIA's interpretative guidelines that allow laboratories the flexibility to determine control procedures that are equivalent to the traditional frequency of two levels of control per day lack a framework for implementing QC across the wide variety of test systems. While flexibility in implementing QC is desirable, additional information is required to implement the guidelines effectively.
 - Several factors may contribute to the inconsistencies in implementing equivalent QC. These include the lack of adequate risk management information from manufacturers, the different types and levels of QC required by each device and method, and the unique considerations of individual laboratories.⁶⁰ CMS, CLSI, and other stakeholders are developing evaluation protocols that will outline principles for validation and provide laboratories with scientific guidance on the development of QC procedures for specific testing technologies and environments.⁶¹
- Available evidence on the long-term impact of PT on laboratory performance is limited, and findings of existing studies are confounded by limited comparable data from CMS and survey organizations and other methodological shortcomings. Existing studies indicate generally improved performance in recent years.

- Laboratories with PT performance scores of 80% or higher for most specialties and subspecialties are considered successful. As such, PT statistics suggesting satisfactory laboratory performance may fail to detect significant proficiency problems in particular areas. Similarly, the PT results do not necessarily indicate that a laboratory's proficiency is sufficient to meet the needs of the clinician. CMS would increase transparency of PT if it were to consider new ways to code certain tests for PT purposes, including disaggregation of tests within specialty areas, such as microbiology.
- Several efforts are underway to improve the quality of cytology PT programs. CLIAC and CMS are emphasizing the importance of rigorous review and field validations studies of cytology slides used by PT programs. CLIAC recommended changes to the regulations in several areas, such as use of new technology (virtual media), testing frequency, number of challenges, and a grading scheme.⁵¹ Legislation (H.R. 1237) also has been reintroduced.
- Consistent with GAO recommendations, CLIA oversight is being improved by standardizing reporting of survey deficiencies and strengthened enforcement of regulatory obligations.
 - Many laboratories have more stringent quality management programs than are required by CLIA. These programs provide opportunities for laboratories to adapt and validate quality improvement interventions or aspects of these programs. In the short term, these may be incorporated into improved voluntary guidelines and perhaps eventually into an improved regulatory framework.
- Technological advances have made laboratory tests easier to use and less subject to user error, resulting in considerable growth in the number of waived tests since the advent of CLIA. From the nine tests or examinations waived in 1993, approximately 1,600 waived test systems that measure 76 analytes are now waived under CLIA.
 - The large proportion of clinical laboratories that are certified have wide access to tests in this category. Tradeoffs include easier access to recommended testing, with benefits for individual and population health, versus the potential for waived tests to fall short on specimen adequacy, test reliability and accuracy.
- Traditional oversight of LDTs under CLIA for analytical validity may be insufficient for genetic tests for which clinicians and patients seek assurances of efficacy and protections against potential harms. CLIA requirements for LDTs and FDA requirements for the 510(k) and PMA review processes serve different purposes and rely on different data. In general, CLIA emphasizes testing accuracy (i.e., analytical validity, not clinical validity) and FDA emphasizes safety and efficacy (clinical validity and, in some instances, clinical utility). Most genetic tests are LDTs and therefore are subject solely to CLIA regulations. Only a small number of genetic tests are regulated as IVD test kits or systems subject to premarket review by FDA for safety and efficacy via the 510(k) or PMA processes.
 - The extent to which FDA has actively regulated certain LDTs is changing. Guidance documents issued by FDA in 2006 and 2007 pertaining to ASRs and IVDMIAs indicate a noteworthy shift of regulatory oversight for a small, yet growing number of complex tests. The guidance is likely to expose these tests to increased scrutiny similar to premarket review via the 510(k) or PMA processes.

- Although they account for a small proportion of all tests performed by clinical laboratories, more than 1,000 genetic tests are available for clinical use, with hundreds of others used in research settings. PGx testing is a relatively new form of genetic testing; to date, only a few such tests are used to support decisions for selecting and dosing therapies.
 - CMS announced in September 2006 that it would not pursue a Notice of Proposed Rule Making for genetic testing, but that it would implement an action plan for enhanced oversight of genetic testing under existing CLIA authority. Elements of the action plan include expanded training of surveyors, collaboration with CDC to publish educational materials, development of alternative PT mechanisms, and coordination with CDC and FDA on oversight activities. CMS also is working with SACGHS, FDA, and other experts to address current gaps in oversight of laboratories that conduct genetic testing and to otherwise support or augment its action plan.
 - As genetic testing and PGx, in particular, evolve, there is an ongoing need for guidance from CMS and FDA regarding respective scopes of regulatory oversight pertaining to these tests. Manufacturers of tests and therapies whose safety and effectiveness are mediated by genetic factors will seek ongoing guidance from FDA for co-development of drugs and diagnostics and related regulatory matters pertaining to PGx.

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CHAPTER VIII

REIMBURSEMENT FOR LABORATORY MEDICINE

Reimbursement for most health care in the U.S. is administered by government and private sector third parties using multiple systems of coverage, coding, and payment. Third-party payment has enabled patients to access and benefit from health care products and services, including laboratory testing, and ensures broad markets for these. However, difficulty in acquiring coverage, appropriate coding, and adequate payment can pose significant hurdles to laboratory testing. The consequences can include reduced patient access to laboratory testing and decreased incentives for laboratories and test manufacturers to engage in further test development.

As health care continues to usurp a larger proportion of national spending, it places greater burdens on employers, patients, and the health care system itself, with broader implications for industry, competitiveness, and other aspects of the economy. These pressures are leading to proposals to modify and even broadly reform health care payment systems.^{1,2,3}

Many of the concerns pertaining to Medicare payment for laboratory services were identified in the 2000 IOM report, *Medicare Laboratory Payment Policy: Now and in the Future*.⁴ Yet, little has changed since publication of that report. This chapter provides an overview of the current public and private sector payment systems for laboratory services and an analysis of payment issues that affect laboratory testing access, effectiveness, efficiency, and innovation.

PUBLIC AND PRIVATE SECTOR PAYERS

The U.S. health system has multiple public and private sector payers. CMS is the largest purchaser of health care in the U.S. CMS administers Medicare, a federal program, and the federal portion of the Medicaid program and the State Children's Health Insurance Program, which are funded jointly with the states. In fiscal year 2006, CMS net outlays were approximately \$515.2 billion for these programs,^a about 19.4% of total federal outlays.⁵

Medicare provides benefits for 43.2 million beneficiaries, including 36.3 million elderly and 7 million disabled enrollees, comprising 14% of the population. By 2031, the number of beneficiaries will be an estimated 77 million.⁶ This includes the baby-boom generation, the last of which will turn 65 in 2029. The Medicaid program covers 50.3 million beneficiaries, about 17% of the U.S. population. More than 75% of Medicaid enrollees are low-income children and their parents.⁶

Other government payers, i.e., the Military Health System (MHS), VHA, and Indian Health Service, operate independent health care systems that provide services directly to their beneficiaries or through negotiated contracts with private sector providers. In fiscal year 2006, the MHS and VHA programs were estimated to spend \$70 billion on health care for approximately 16 million enrolled veterans, active duty, and retired military personnel and their beneficiaries.^{7,8}

^a The other federal outlays included Social Security \$586 billion (22%), defense \$499 billion (18.8%), treasury \$464 billion (17.5%), and other \$590 billion (22.2%).

Private sector payers include insurance companies and commercial health plans such as Aetna, Blue Cross and Blue Shield plans, CIGNA, Kaiser Permanente, UnitedHealthcare, and WellPoint. Some of these plans also act as contractors to Medicare and Medicaid, processing claims and administering payments to laboratories. In 2005, approximately 200 million Americans were enrolled in managed care plans, including 15 million enrolled in Medicaid programs, and 7 million in Medicare programs.^{9,10}

Based on 1999 data reported by the IOM, clinical laboratories derive their revenues from fee-for-service payments (42%), followed by Medicare payments (29%), Medicaid payments (12%), consumers' out-of-pocket payments (10%), and health maintenance organization (HMO) capitation payments (7%).⁴

Components of Reimbursement Systems

Three main components of payment systems are coverage, payment, and coding:

- **Coverage decisions** establish the conditions under which third-party payment is provided, including the range of benefits provided under particular plans or contracts, which items and services can be reimbursed under those benefits, clinical indications for which these items and services (e.g., laboratory tests) will be reimbursed, and the circumstances or settings in which the items and services will be reimbursed. Medical necessity and appropriateness determinations affect payer coverage decisions.
- **Payment methodologies** establish payment levels for tests and services provided and methods for calculating these amounts. Payment levels typically are tied to the codes for these tests and services. These levels may be provided in the form of prospective payment systems (PPSs), fee schedules, or negotiated contracts with payment rates for particular codes. The type of payment methodology of choice may vary by insurer.
- **Coding systems** involve the alphanumeric nomenclatures assigned to particular health conditions, services, or products and the processes for assigning and updating these. The coding systems that apply to laboratory medicine include Current Procedural Terminology® (CPT) codes and Healthcare Procedural Coding System (HCPCS) codes for laboratory tests and services and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for diagnoses.

Coverage and coding policies shape the operation of payment systems. Whether for laboratory testing or other types of health care, the design and implementation of payment systems can influence patient access, provider decision-making, and innovation.

COVERAGE DECISIONS

Public and private sector payers make coverage decisions independently, often with consideration of the financial impact resulting from specific determinations. However, legislative actions may mandate coverage of specific tests by all payers.

Medicare Coverage Decisions

Medicare's authorizing legislation in 1965 established broad categories of coverage for hospital, physician, and laboratory services, but limited payment to expenses deemed reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.¹¹ Coverage decisions are left to Medicare officials who, in turn, have delegated most of their authority to local contractors, which are typically private sector insurance companies that administer the program in specific geographic jurisdictions, subject to national Medicare provisions and requirements.¹²

The contractors that administer Part A of Medicare are known as fiscal intermediaries (FIs) and those that administer Part B are known as carriers. About 90% of all Medicare coverage reviews and decisions still occur at the local level while 10% occur at the national level. In 2007, there were 16 carriers and 20 FIs. However, for laboratory services, there are 56 carriers for corresponding geographic areas (see payment section below). Carriers handling other Part B services can serve as one of the 56 carriers handling laboratory services.

Most Medicare coverage policies for new tests and services under Part B are established by local carrier advisory committees and are known as local coverage determinations (formerly referred to as local medical review policies). In this decentralized system, there is substantial variation among coverage policies of different carriers. Aside from the uncertainty and inconsistency that arise from this arrangement are long-standing concerns regarding the lack of openness, transparency, predictability, and length of time involved in these coverage processes.¹¹ In addition, the Medicare statute restricts payment for preventive and screening services and technologies, unless otherwise specified by Congress.

Several legislative initiatives, along with various policy reports, have been directed at some of these issues. The Balanced Budget Act of 1997 provided the legislative vehicle to consolidate the number of CMS contractors making coverage decisions and processing laboratory claims from 56 to 5.¹³ However, the consolidation has not been implemented to date. In 1999, CMS established the Medicare Coverage Advisory Committee (now called the Medicare Evidence Development and Coverage Advisory Committee) and restructured the national coverage processes in order to facilitate more systematic and transparent national coverage determinations for Medicare. The Medicare Evidence Development and Coverage Advisory Committee provides recommendations based on literature reviews, technology assessments, and expert advice, though CMS retains control over final decisions.¹¹ National coverage determinations take precedence over local carrier decisions. Although it continues to improve, CMS has failed frequently to meet its standard for prompt assessment of six to nine months, depending on the type of test or technology. Review times for some decisions frequently exceed nine to twelve months.¹⁴

In 2001, the Medicare Payment Advisory Committee (MedPAC) recommended the elimination of local coverage policies and payment schedules in order to reduce complexity, inconsistency, and uncertainty associated with Medicare reimbursement.¹⁵ (MedPAC is an independent federal body established by the Balanced Budget Act of 1997 to advise the U.S. Congress on issues affecting the Medicare program.) However, this proposal was resisted by many stakeholders, including those affiliated with laboratory medicine. In response to concerns from the laboratory community, CMS published a negotiated proposed rule making in 2001 to implement 23 national

coverage policies for 66 CPT codes that represent about 60% of all laboratory tests billed to the Medicare program (see Box 8.1).¹⁶ The national policies describe the medical conditions for which a laboratory test is covered and set frequency limits on coverage of the same test for a patient. The rule making also established opportunities for stakeholder involvement in the decision-making process during annual reviews of coverage policies. Even so, some stakeholders continue to call for further transparency in this process.

Under provisions in the MMA 2003, CMS began reforming the carrier-based approach to administration of its programs. This initiative is expected to have a direct impact on the number of carriers affiliated with coverage and processing of laboratory claims. CMS is transitioning to the Medicare Administrative Contractor (MAC) system that will eventually replace all carriers and FIs. The first MAC contract was awarded in July 2006 to Noridian Administrative Services (Fargo, ND) to implement consolidated claims processing for Medicare Part A and Part B in Jurisdiction 3 (Arizona, Montana, North and South Dakota, Utah, and Wyoming).¹⁷ However, at present, the use of MACs will not change the geographic-oriented payment rates or number of fee schedules for laboratory services.¹⁸

In 2003, GAO issued a report that also recommended elimination of local coverage and expansion of the national coverage system. However, as noted in the GAO report's summation of public comments, DHHS and certain stakeholders, including some in industry, opposed doing so, stating that the elimination of local coverage would result in net increases in expenditures, mainly due to spending on additional resources to manage national coverage decisions for all services and products.¹⁹ MMA 2003 expanded Medicare coverage of certain screening tests, including for cardiovascular disease and diabetes.²⁰ These tests and other preventive services are recommended for certain population groups by authoritative groups such as the USPSTF and the Advisory Committee on Immunization Practices.²¹

Box 8.1: 23 National Coverage Determinations for Medicare, Effective 2001

Alpha-fetoprotein (AFP)	Human immunodeficiency virus (HIV) testing (prognosis including monitoring)
Blood counts	Lipid testing
Blood glucose testing	Partial thromboplastin time (PTT)
Carcinoembryonic antigen (CEA)	Prostate specific antigen (PSA)
Collagen crosslinks, any method	Prothrombin time (PT)
Digoxin therapeutic drug assay	Serum iron studies
Fecal occult blood test (FOBT)	Thyroid testing
Gamma glutamyl transferase (GGT)	Tumor antigen by immunoassay - CA 125
Glycated hemoglobin/glycated protein	Tumor antigen by immunoassay - CA 15-3/ CA 27.29
Hepatitis panel/acute hepatitis panel	Tumor antigen by immunoassay - CA 19-9
Human chorionic gonadotropin (hCG)	Urine culture, bacterial
Human immunodeficiency virus (HIV) testing (diagnosis)	

Source: Lab NCDs. Baltimore, MD: Centers for Medicare and Medicaid Services, 2007.

Denials and Advanced Beneficiary Notice

Medicare denies claims for laboratory tests when they fail to meet required criteria.^b According to MedPAC, the national claims denial rate for laboratory services in 2002 was 15%, with much higher rates in certain geographic areas.²² A 2006 analysis found that Medicare denial rates for laboratory testing peaked in 1998 (15%) and have been declining since then to 8.8% in 2004.²³ However, this analysis is confounded by the definition of claims denial, which includes both true denials (i.e., services for which payment was never made) and “paperwork” denials (i.e., denials that are ultimately resolved and paid).

Documentation of reasons for claims denials associated with medical necessity determinations have been inconsistent among carriers. To remedy this problem, CMS introduced additional documentation requirements for medical necessity in the late 1990s. However, inconsistencies have persisted. The IOM concluded that regional variations in denial rates for the top 20 laboratory tests (by dollar value) by carrier were attributed to geographic patterns of fraud and abuse, varying interpretation of Medicare rules by local carriers, and low numbers of tests in a particular region that might skew the proportion of denied claims. Thus, while denials associated with fraud and abuse are certainly appropriate, some proportion of denials are associated with unresolved inconsistencies among carriers.⁴

In a fee-for-service reimbursement system, denied claims are the financial responsibility of the laboratories, rather than the physician ordering the test.⁴ While justifiable claims denials can save costs and improve efficiency, those that are subject only to inconsistent decisions or policies, or that are otherwise unjustified, can contribute to the total cost of providing laboratory services because they may increase administrative costs, decrease aggregate revenue for laboratories, and create bad debt expense. Because the laboratory does not have direct contact with the patient in most situations, it must depend on the clinician to recognize that: (1) the laboratory test ordered is subject to medical review, (2) the medical necessity of the test is indeterminate, and (3) the patient’s signature on an Advanced Beneficiary Notice^c (ABN) is needed.⁴ In cases where a patient receives a laboratory test that is not covered by Medicare and for which an ABN was not signed, the laboratory must absorb the cost.²⁵

In 2002, CMS issued an ABN form specific to laboratory testing that allowed laboratories to list tests that could be denied as well as specify the possible reasons for denial.²⁶ To simplify ABN further, in 2007, CMS proposed combining the general use ABN and the laboratory ABN.²⁷ However, many clinical laboratory professional societies stated their preference to retain the separate laboratory ABN form as it provides beneficiaries with a clear understanding of the reasons for the denial of coverage of specific laboratory tests.^{28,29} As of December 2007, CMS maintained both forms; however, laboratory experts anticipate that the agency will introduce and require use of a new, combined form in 2008.³⁰

^b Medicare denies claims for laboratory tests when such claims are for tests that Medicare does not cover, do not meet medical necessity requirements, are for individuals who are not Medicare beneficiaries, are from laboratories that are not Medicare-providers or are not certified by CLIA to perform that particular test, are not documented sufficiently, and are for patients whose primary coverage is from another payer.⁴

^c Medicare requires that physicians notify beneficiaries of the possibility that Medicare might not deem a laboratory test medically appropriate. Beneficiaries must sign an ABN acknowledging their understanding of this policy and personal responsibility for payment.²⁴

Medicaid Coverage Decisions

Medicaid beneficiaries receive a comprehensive set of medical benefits, with some services required by the federal government and others offered at the discretion of the state.³¹ Individual states have substantial decision making authority over which benefits their Medicaid programs will cover. Within the broad national guidelines established by federal statutes, regulations and policies, each state: (1) establishes its own eligibility standards; (2) determines the type, amount, duration, and scope of services; (3) sets the payment rates for services; and (4) administers its own program.³² About 35% of spending in each state is for federally mandated benefits (e.g., laboratory services) while 65% is for optional services (e.g., prescription drugs).³³

Federal guidelines apply to coverage and payment for laboratory services under Medicaid. Medicaid programs are required to cover professional and technical laboratory services that are:

- Ordered and provided by or under the direction of a physician or other licensed practitioner, or ordered by a physician and provided by a referral laboratory
- Furnished by a laboratory meeting the requirements outlined in CLIA³³

This includes laboratory testing conducted in the spectrum of inpatient and ambulatory care settings in which services can be provided to Medicaid beneficiaries.³³ Also, Medicaid must cover screening, diagnostic, and treatment services for beneficiaries under age 21.

All states participating in the Medicaid program must designate one state agency that is responsible for administering and supervising the state's Medicaid program.³⁴ However, federal rules do not dictate a specific administrative structure for state Medicaid programs or how coverage decisions must be made, including those for new laboratory testing technologies. In New York State, for example, various offices within the Department of Health, Governor's Office, the Legislature, and other agencies all play a role in determining what benefits the state's Medicaid program will cover and what models of service delivery it will employ.

TRICARE and Veterans Health Administration Coverage Decisions

Both the TRICARE and VHA significantly expanded their benefit programs in the 1990s. Independently, the programs were reorganized to incorporate policies and procedures used by preferred provider and managed care organizations. For TRICARE, coverage of health care services, including laboratory services, has remained constant and generous. Because TRICARE provides care to family members of military personnel, a full spectrum of diagnostic services are available as part of the benefits package, including many genetic tests used to screen and diagnose newborns through adults.

The VHA provides a standard health benefits plan to enrollees; however, unlike TRICARE, it does not provide benefits to family members. The plan emphasizes preventive and primary care, and offers a full range of inpatient and ambulatory care services within the VA health care system, including laboratory tests for screening, diagnosis and treatment. Funding of the program is discretionary and the system is expected to meet the needs of its beneficiaries within its budget, although Congress may authorize additional funds if needed.

Private Sector Coverage Decisions

Most private payers maintain their own process for making decisions regarding coverage, although they often follow the coverage decisions made by Medicare and some of the larger private health plans.^{10, 35-37} Similar to government payers, coverage decisions are made at the local level; however, in contrast, private payers are not obligated to establish advisory committees or engage in publicly open processes.³⁸ Private payers may choose to adjust policies following introduction of new technologies to the market, with the impetus for such changes coming from a variety of sources, such as state or federal mandates, consumer preference, or financial concerns.^d In addition, payers may negotiate specific coverage plans with the groups or employers purchasing the plan.³⁹

Constraints on health care costs, demand for better outcomes and higher quality, and the unprecedented rate at which new technologies are being introduced to the market have driven many health care payers to use evidence-based decision-making to determine the most appropriate services and technologies to cover.³⁵ Public and private sector payers increasingly draw upon health technology assessments (HTAs) to inform their coverage decisions. HTAs typically involve using a systematic approach to assembling and interpreting available evidence to determine whether a test or medical service is safe, effective, and, sometimes, cost-effective, for particular patients and health care settings. Several payers have conducted health technology assessments for screening, diagnostic, and monitoring laboratory tests.

Some health insurance plans and purchasers have created thorough processes for conducting HTAs internally. Those that do not conduct formal reviews of new technologies may purchase assessments from HTA vendors. Examples of private health plans that conduct formal reviews of new technologies include Aetna, CIGNA, UnitedHealthcare, and WellPoint.¹⁰ Various HTA vendors in the U.S. generate proprietary assessments that are available to payers and other subscribers. For example, the Technology Evaluation Center (TEC), established by the Blue Cross Blue Shield Association, produces evidence-based technology assessments of the clinical effectiveness and appropriateness of a specific medical procedure, device, or drug.^{40, 41} TEC is guided by its Medical Advisory Panel, which consists of 19 independent, nationally recognized experts in HTA, clinical research, and medical specialties.⁴² ECRI^e and HAYES, Inc.^f are two other examples of U.S.-based HTA vendors whose reviews are used by payers in support of their coverage decisions.^{43, 44}

^d Health insurance plans are required by law to provide information to plan members about what services are covered and how coverage decisions are made and can be appealed. Denied claims must be accompanied by a reason for the denial, including citations of any policy or criteria on which the coverage decision is based.³⁵

^e ECRI Institute is a nonprofit organization that provides consulting services related to, e.g., patient safety, quality, risk assessment and management, and technology assessment. It is also an AHRQ-designated Evidence-based Practice Center.

^f HAYES, Inc., provides technology assessment reports for health plans, managed care companies, hospitals, and health networks and offers training programs to facilitate participants' understanding of the HTA process.

Laboratory tests that have been assessed by the TEC include:

- Serial endpoint testing for the diagnosis and treatment of allergic disorders
- High-sensitivity C-reactive protein measurement for coronary heart disease risk stratification
- iFOBT vs. gFOBT
- Use of intermittent or continuous interstitial fluid glucose monitoring in patients with diabetes mellitus
- Use of epithelial cell cytology in breast cancer risk assessment and high-risk patient management
- Chemotherapy sensitivity and resistance assays⁴⁰

In addition to HTA findings, private payers also may consider clinical practice guidelines, cost, and the availability of an appropriate CPT code.³⁵ Private payers are becoming more open to meeting with manufacturers to discuss what data they need to make coverage decisions for new technology.³⁹ In general, there is consistency in coverage among private sector payers in routine laboratory testing associated with standard of care, although some remaining variations in coverage may inhibit an individual's access to certain tests and services.¹⁰ The 2006 SACGHS report on coverage and payment for genetic tests and services found that, of those private payers whose coverage policies are publicly available, most cover genetic testing for chromosomal abnormalities, prenatal and neonatal diagnosis, and pre-implantation genetic diagnosis in some cases.³⁵ These payers also generally cover genetic testing for certain rare diseases.

Less information is available regarding denial rates for private payers. One indication of denial rates comes from Athenahealth, Inc., a provider of web-based services and software to medical practices, whose "PayerView" program reviews health insurance performance from the perspective of physicians.⁴⁵ In 2006, Athenahealth published its first "PayerView" for of Texas, which analyzed claim performance data for more than 330 providers and 59 medical practices. Medicare Part B in Texas denied 5.6% of claims submitted, which was below the rate for the state's private insurers, which ranged from 6.5 to 10.4% among the top eight companies.

Outstanding Issues in Coverage

Limited Medicare Coverage of Screening Tests

Medicare is limited by statute to providing coverage only for items or services that are "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." In order for Medicare to cover screening or preventive interventions (i.e., in patients without signs, symptoms, complaints or personal history of disease or injury), Congress must pass new legislation mandating coverage of those specific interventions. Examples of preventive tests approved by Congress to date include tests to screen for cardiovascular disease, cervical and vaginal cancer, colorectal cancer, breast cancer, prostate cancer, glaucoma, osteoporosis, abdominal aortic aneurysm, and diabetes.⁴⁶ In addition, Congress has also approved Medicare coverage of smoking cessation counseling, medical nutrition therapy for beneficiaries with diabetes or renal disease, vaccinations to prevent influenza, pneumonia, and hepatitis B virus, and a one-time "Welcome to Medicare" physical examination for new enrollees. In contrast,

coverage of preventive services and screening tests is quite extensive for private sector payers. The Medicare Preventive Services Coverage Act of 2007 (S. 2115), introduced in Congress in September 2007 by Senator Ben Cardin (D-MD), includes provisions for expand Medicare coverage for certain preventive tests and related services. (See Box 8.2.)⁴⁷

Box 8.2: Medicare Preventive Services Coverage Act of 2007 (S. 2115)

The bill's core provisions call for Congress to:

- Extend the eligibility period of the "Welcome to Medicare" visit, a preventive physical examination, from 6 months to 1 year
- Authorize the Secretary of DHHS to expand Medicare coverage to include services deemed reasonable and necessary for the prevention or early detection of illness or disability, taking into account evidence-based recommendations by the USPSTF and other appropriate organizations
- Eliminate coinsurance rates for the "Welcome to Medicare" visit and other preventive services^{47, 48}

Source: S. 2115: The Medicare Preventive Services Coverage Act of 2007.

Inconsistencies in Coverage of Genetic Tests among All Payers

Some emerging tests (e.g., those used in PGx) may not fit neatly within Medicare's coverage criteria. Medicare considers most predictive and predispositional genetic tests to be screening tests, and as such, congressional authorization is necessary for coverage. Most genetic tests are not covered by Medicare unless they are performed on symptomatic individuals or are used to identify treatment-responsive populations.⁴⁹ Unresolved issues pertaining to coverage of genetic tests include: (1) the extent to which genetic tests used in broader metabolic profiles, or for more limited profiles targeted to specific biomarkers meet current medical necessity criteria; and (2) the extent to which genetic tests can be tied to clinical decision making and patient health outcomes.⁵⁰

In 2006, SACGHS recommended that Medicare cover predictive and predispositional genetic tests and their accompanying services (e.g., genetic counseling) that meet appropriate evidence standards.³⁵ SACGHS also recommended that CMS clarify that a "personal history" of disease can include having a family history of a disease, thereby making it possible for beneficiaries with a family history of a disease to meet Medicare's standard of "reasonable and necessary."

With the exception of newborn genetic screening and follow up, which are federally mandated, states are responsible for Medicaid coverage decisions for genetic tests and services.³⁵ Given individual state differences in policy, there is significant disparity in patient access to these tests and services. States' decisions regarding whether to cover specific genetic tests is determined in large part by financial and political factors. Although Medicaid programs account for, on average, about 22% of state budget, states sometimes restrict Medicaid spending by limiting coverage and/or payment rates, particularly on those items and services outside the scope of federal requirements.^{51, 52} In 2006, SACGHS recommended that DHHS ensure that all states receive information about genetic tests and services in order to inform their Medicaid coverage decision making processes.³⁵

Coverage for newly developed tests, especially molecular, genetic, and PGx tests, varies widely among private sector payers. Often, there are fewer research studies^g available on their clinical utility and costs.^{10, 35, 39, 53} In 2004, the Congressional Research Service reviewed the coverage decisions of 27 private payers and found that 16 had developed policies for genetic testing to detect hereditary colon cancer.⁵³ However, coverage decisions for this testing varied widely across individual payers.^h

The variability in coverage has arisen in part because neither public nor private payers have developed uniform methods for obtaining information from laboratories about the new tests.⁵⁴ The lack of a uniform process for making coverage decisions can lead to inappropriate use (e.g., overuse and underuse) of new laboratory testing technologies that otherwise have the potential to improve the quality of health care.¹⁰ Recently, some public and private sector stakeholders have recognized the need to provide guidance to private payers in the areas of PGx and genetic testing. In 2006, SACGHS recommended the establishment of a task group that includes public and private sector representatives to create a set of guiding principles for coverage decisions, addressing issues such as economic evaluation/cost-effectiveness, prevention, rare disease tests, therapeutic benefit, and informational utility, and make available all scientific evidence needed to support private payer coverage decisions for individual patient populations served by the respective payer.

PAYMENT METHODOLOGIES

Although private sector insurance accounts for higher revenues, it is the Medicare program that exerts the strongest influence on laboratory services payment for all payers. According to a microcosting study performed for an IOM report, 66.7% of private insurance plans evaluated for the study used the Medicare payment rates as the basis for their own.⁵⁵ The Medicare payment rates also affect state Medicaid programs and other federal payer programs. As such, various strengths and weaknesses of the Medicare payment system extend beyond Medicare to other payers, providers, and beneficiaries.

Medicare Payment Methodologies

The current payment structure of the Medicare program comprises multiple, often complex payment methodologies for Part A (inpatient care), Part B (hospital outpatient and ambulatory care), and Part C (private sector options), depending on site of care and services provided. Part A pays for inpatient hospital, skilled nursing facility, home health, and hospice care. (See Appendix C for additional information on the development of the Medicare payment system.) In 2006, Part A accounted for 41% of Medicare spending, Part B accounted for 35%, Part C accounted for 16%, and the new Part D prescription drug benefit accounted for 8%.⁵⁶

^g Although demonstrating improved health outcomes is a primary factor in coverage determinations, the effect of molecular and genetic test results on a patient's health may not be realized for many years, making it difficult to perceive and measure the immediate benefits and long term cost effectiveness of such tests.³⁹

^h Four payers covered genetic testing without specifying the genes, five covered mutation analysis in three common genes, four covered microsatellite instability analysis in addition to the standard genetic tests, one covered genetic testing of only one gene, and two did not cover genetic testing at all.

Rising costs of care and pending retirement of the baby boom generation suggest accelerated growth in Medicare outlays in 2010 and beyond. Over the past 40 years, costs per beneficiary under Medicare and Medicaid have increased about 2.5% faster per year than has per capita gross domestic product.⁵⁷ Medicare spending is projected to grow at a rate of 7.3% over the next decade.⁵⁸ Congress has directed federal agencies, particularly payers, to study possible alternatives to the current payment methodology (such as competitive bidding) as well as more aggressive strategies to cut costs.

Prospective Payment Systems for Inpatient and Hospital Outpatient Care

For inpatient care under Part A, payment is provided via lump sum based on the patient's diagnosis. Hospital diagnosis-related groups (DRGs) are designed to cover institutional costs, excluding physicians' services that are paid for through the Part B fee schedules. Included in the DRGs are any laboratory tests that are bundled with other services for a given hospital admission. Other inpatient facilities use prospectively set groupings that are similar to DRGs; some use per diem rates.¹ Generally, a standardized base rate is determined according to the diagnosis grouping and associated relative value, which may be adjusted to accommodate case-mix (i.e., health condition, clinical characteristics) and geographic differences in wages. (Relative value payment methodology is discussed below.) For hospitals, additional adjustments can be made to sites treating a disproportionate share of low-income patients, sites in rural locations, or outlier cases of extraordinarily high cost.

Both operating and capital payment rates are updated annually for all PPSs. Operating costs are updated according to the projected increase in CMS' market basket index (which measures price increases of goods and services hospitals buy to produce patient care). Capital updates are determined by the Secretary of DHHS. In addition, payments to hospitals that fail to provide data on specified quality indicators are reduced by 2%.⁵⁹ (Reporting on quality indicators as a condition to maintain payment level is not required of other inpatient facilities at this time.)

The change to PPSs for inpatient care had a significant effect on clinical laboratories. Until 1984, hospital laboratories generally were recognized as profit centers. However, the institution of prospective payment based on DRGs and similar capped payment rates transformed inpatient laboratory testing into a cost center, creating incentives to reduce the number of tests ordered as well as to shift inpatient care to the hospital outpatient and ambulatory care settings.⁴ When DRGs were introduced, CMS assumed that the mean cost attributable to the laboratory as a proportion of the revenue generated by DRGs would not exceed 9.5%.⁶⁰

The proportion of payment attributed to laboratory tests is mediated, in part, by the patient's health condition. A 2000 report of a study that examined 486 DRGs drawn from a large University HealthSystems Consortium database found that the proportion of payment associated with laboratory tests and services averaged 6% for surgical DRGs and 9% for other DRGs designating the management of medical conditions.⁶¹ The highest proportion of total costs attributable to the laboratory was 18.3% for acute leukemia, 13.6% for HIV with surgical procedure, and about 8 to 10% for various transplant procedures. Tests for kidney and urinary signs and symptoms in children also were higher than average. Median laboratory costs were

¹ Separate Medicare PPSs have been developed for other for health care facilities, including skilled nursing facilities, long-term care, hospice care, inpatient psychiatric care, home health and inpatient rehabilitation.

<1.0% for only 15 DRGs. Since the publication of this study in 2000, there has been little research on the contribution of laboratory costs to total costs or the effect of variations in laboratory costs on quality of care.

In August 2000, CMS began using an outpatient prospective payment system (OPPS) for outpatient hospital care in order to restrain cost increases. This system provides a fixed, prospectively determined, bundled payment for products and services provided by hospitals in outpatient settings, excluding those services provided by physicians and other health care providers.⁶² Similar to DRGs, the OPPS classified services into ambulatory payment classifications (APCs). All services within a given APC are assumed to be clinically comparable and have comparable resource requirements, and therefore, have the same payment rate. APCs pertain to laboratory tests, implantable devices, items used in diagnostic radiography, and durable medical equipment (DME) associated with hospital outpatient services.⁶³ Physicians' fees, including those for certain pathologist-related consultative services, are paid through the Part B fee schedule. (Splitting of laboratory fees into physician fees and "technical components" paid differently is discussed in the next section.)

Along with bundling, the move to OPPS significantly affected the ways that independent laboratories can bill for their services. Independent laboratories that provide pathology services to registered hospital outpatients must bill the hospital directly for the technical component. The hospital receives payment from Medicare under Part A and the independent laboratory receives payment from Medicare for pathologist fees.⁶⁴ Laboratory professional organizations have opposed the OPPS, citing concerns about administrative and financial burdens on hospitals and clinical laboratories.⁶⁵ Stakeholder actions prompted the inclusion of an exception in the Benefits Improvement and Protection Act of 2000.⁶⁶ The legislation allows independent laboratories with contracts in place by the date of the proposed rule-making to continue to bill Medicare directly for technical component services.

Health care facility costs associated with blood banking and transfusion medicine are paid via the inpatient and outpatient PPSs. Fees for services associated with end stage renal disease are paid via the outpatient dialysis services payment system.⁶⁷ This system uses a composite rate that is intended to cover the bundle of services, laboratory tests, certain drugs, and supplies that are routinely required for dialysis treatment. Providers must bill Medicare separately for certain injectable medications and laboratory tests that are not included in the bundle.

Other government payers, i.e., Medicaid, TRICARE, VHA, use the Medicare DRGs, with some modifications, for payment of inpatient and hospital outpatient services for their respective beneficiaries.⁶⁸⁻⁷⁰ However, Medicare Part C (in which CMS contracts with health plans to provide care to Medicare beneficiaries), TRICARE, and the Federal Employee Health Benefits have switched from PPSs to competitive bidding contracts.⁷¹

The change to PPS by Medicare prompted a similar move by private sector. Private payers typically use one of several PPS methodologies for inpatient and outpatient hospital settings, such as all-inclusive case rates, per diem rates, and DRGs.¹⁰ As is the case with the Medicare PPS, all-inclusive rates used by private payers do not provide separate payment for each resource used. These PPSs rely on their ability to capture or accurately estimate how much each resource costs in order to account for it when determining payment rates. Private payers usually use the Medicare DRG groupings, but will assign their own relative weights to the individual DRGs. While the

payment amounts negotiated between the hospital and the payer have been proprietary information, at least one major private payer recently announced that it will make public the actual payment rates negotiated with physicians.^{72, 7372, 73}

Fee-for-Service Payment Systems for Ambulatory Care

Public and private sector payers cover ambulatory care and other services such as laboratory tests according to predetermined, fixed fee schedules, negotiated contracts, or competitive bidding contracts.

A fee schedule is a list of allowable fees representing the average or maximum amount that the payer will reimburse providers for the service.⁶⁹⁶⁹ HCPCS codes, including CPT codes, describe specific tests or services and link the service to the fee schedules. Medicare uses three fee schedules under Part B to provide payment for a given service, procedure, or item. Most private sector payers base their fee schedules on the Medicare schedules.

- (1) *Medicare physician fee schedule (MPFS)*. This fee schedule covers physician and other licensed health care practitioner services, including office visits, surgical procedures and certain laboratory services that require professional interpretation, such as anatomic pathology tests and certain gene-based, molecular or similarly complex tests. Physician services can occur in different settings. Determinations of the payment rate are based on three aspects affecting physician services: physician work, practice expense (all costs other than physician time required for the physician to provide the service), and malpractice expense.
- (2) *Clinical laboratory fee schedule (CLFS)*. Medically necessary diagnostic and monitoring laboratory tests and, with recent legislation, certain preventive and screening tests, are reimbursed according to fee schedules differentiated by geographic region and the national limitation amounts (NLAs). Testing and services may be furnished by hospital, independent, or physician office laboratories, which bill Medicare directly for tests performed. Technologies covered under the CLFS include diagnostic test kits and reagents, devices that analyze test results, and other laboratory equipment essential to testing.
- (3) *Durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS)*. Medicare pays for non-implantable DMEPOS through this fee schedule, although some types of equipment are paid on a reasonable cost basis, such as dialysis supplies and equipment. While the DMEPOS fee schedule does not directly affect payment for laboratory services, cost containment strategies used for DMEPOS are being examined to cut costs associated with the CLFS.

Using Fee Schedules for Laboratory Tests and Services

Use of the MPFS, CLFS, and other payment methods varies according to test type. Payment for anatomic pathology tests and certain clinical pathology and highly complex molecular or gene-based tests have two components – a professional component and a technical component. The professional component covers the costs of interpretive consultation when the pathologist discusses test results with the patient’s clinician. The technical component covers specimen collection, transport, processing, preparation (e.g., centrifugation, tissue block cutting), analysis (e.g., automated, microscopic exam), and storage.

While all covered anatomic pathology tests are afforded payment for consultative services, only a few clinical pathology and molecular and genetic laboratory tests can be reimbursed for consultations. For anatomic pathology tests, both the professional and technical components are paid according to codes on the MPFS. For clinical pathology, including molecular and gene-based testing, both components are paid via codes on the CLFS.

Medicare Physician Fee Schedule

The MPFS is a set of physician services and payment rates tied to CPT codes. A resource-based relative value scale is the methodology used to classify and calculate the physician payment rates. Physician payments in the fee schedule are calculated by ranking medical services (as defined by CPT and other HCPCS codes) according to the relative costs of resources required to provide them. Physicians who treat Medicare patients are paid for their services through the MPFS, including those providing inpatient, hospital outpatient, and other ambulatory care.^j This includes pathologists associated with laboratory tests and services.

Payment rate calculations involve several steps. First, for each CPT code, CMS assigns a relative value^k that is weighted based on three factors: (1) the amount of work required to provide the service (e.g., differences in time and intensity of work between a physician exam and surgical procedure), (2) expenses related to maintaining a practice (e.g., supplies, staff), and (3) malpractice liability insurance costs. Each factor's relative value is the national average determined through periodic national surveys sponsored by CMS.^l Second, the relative values given to each factor are adjusted for geographic differences in input prices. Separate geographic practice cost indexes are used for this purpose. Third, the sum of the relative values (of the three factors) is multiplied by the standard dollar amount (the fee schedule's conversion factor) to arrive at the payment amount for a particular service.⁷⁴

Unlike the CLFS, the MPFS is updated regularly. The relative values are updated every five years at a minimum. The conversion factor updates payments for physician's services annually according to a formula-based sustainable growth rate (SGR).⁷⁴ The SGR sets a target^m for growth in Medicare spending on physician services (per volume growth) that is no greater than growth in the national economy, after accounting for percent changes in enrollment in the Medicare program.⁷⁵ The annual update to the MPFS depends on comparison to the target. If spending is below the target, the fee update for the next year is increased. Conversely, if actual spending exceeded the target, the fee update is reduced. If spending exceeds the target by a large enough amount, fees will be cut for one year, up to a maximum of 7% below the underlying rate of inflation. Since 1995, fee increases have averaged 2.5-3.0%.

^j For most physician services, Medicare pays 80% of the MPFS amount and the beneficiary is responsible for the remaining 20% as coinsurance. Additional modifiers may be used to adjust the payment depending on the type of service provided, type of clinician providing the service, and whether or not a physician participates in the Medicare program or is working in an underserved area.

^k The relative value unit is a unit of measure designed to permit comparison of the amount of resources required to perform various provider services by assigning weights to such factors as personnel time, level of skill, and sophistication of equipment required to render service.⁶⁹

^l Payments for physician assistants, nurse practitioners, and nurse midwives also are tied to relative value amounts.

^m Four factors define the target: (1) long-term trend in U.S. real gross domestic product per capita; (2) growth in the Medicare fee-for-service population; (3) increases in Medicare fees (payment rate, conversion factor); and (4) the impact of changes in law and regulation (e.g., additional costs due to expansion of benefits to include more screening services).²³

In recent years, overall growth in Medicare spending on physician services has significantly exceeded the SGR target, although growth in spending on laboratory tests during 2000-2004 (10.8%) was consistent with that of all SGR-covered services (11%).²³ Steep physician fee cuts were planned for 2003. However, after strong opposition by physician groups, Congress agreed to consecutive, conservative increases of 1.5% for 2004 and 2005. More recently, the planned cuts of 4.4% for 2006 were replaced with a one-year price freeze. Given the multitude of factors affecting Medicare's sustainability, continued use of the SGR in its present form could result in physician fee cuts of 4-5% per year (the result of 2-3% inflation less the 7% penalty, according to one analysis.²³ However fee cuts of this magnitude have only occurred once before in 2002. The matter of revising the SGR formula remains a central issue pertaining to the MPFS.

CMS' last estimate of laboratory practice expenses was reported in 2003.⁷⁶ The supplemental expense data for this estimate was obtained from a survey conducted by CAP of independent laboratories reporting physician hours and expenses associated with anatomic pathology.ⁿ The survey found that the total practice expenses in anatomic pathology per physician hour at independent laboratories averaged \$160.50. Although this amount was substantially higher than the all-physician average practice expense per hour and was at the upper end of the distribution of practice expenses per hour across all specialties, an objective auditor found that the data submitted for the survey met formal CMS requirements for supplemental practice expense data. On the basis of its review, the auditor recommended that CMS use these values in its calculation of 2004 practice expense relative value units for the 2004 MPFS. This implies that the costs to provide laboratory services are higher than for other medical disciplines.

Clinical Laboratory Fee Schedule

Independent laboratories, POLs, and hospital laboratories when functioning as reference laboratories (except hospital outpatient services) receive payment for their services through prospectively set payment rates. Payment rates are tied to laboratory services listed in HCPCS. The main factors that influence payment include: (1) prevailing charges; (2) national limitation amounts; (3) annual updates; and (4) entry of new technologies.

Prevailing charges. Medicare pays laboratories directly for services performed in the ambulatory care setting through the use of the 56 fee schedules that coincide with geographic areas and designated carriers that process claims. These fee schedule amounts differ from carrier to carrier. The original fee schedules were established by Congress in 1984. Although the original intent was to move toward a single, national fee schedule, efforts to do so have been repealed repeatedly over the years.

Payments for each laboratory test were set separately for each carrier's geographic market based on a percentage of the prevailing charges for 1983. Specifically, the 75th percentile of the carrier customary charges defined the prevailing charge for a given area. The payment rate for hospital laboratories was set at 62% of the prevailing charge (reduced to 60% in 1987), while the rate for independent laboratories and POLs was set at 60% of the prevailing charges. Because some carriers' charges were significantly lower, the rules also include a provision mandating that all laboratories be paid the lower of submitted charges or the fee schedule rate.

ⁿ The survey asked respondents to exclude physician hours and expenses related to clinical pathology services.

National limitation amounts. Beginning in 1986, Congress established upper limits on laboratory payment rates, known as NLAs, at 115% of the median of all carrier rates for each test. Since their institution, NLAs have been reduced seven times, and have remained at 74% of the median for the past decade.¹² The actual payment paid to laboratories is the lowest of the providers' charge, carrier's fee schedule amount, or NLA. Most laboratories are paid at or close to the NLA.

According to the 2000 IOM report, 85% of all pricing amounts across the 56 carriers and more than 1,100 test codes were subject to NLAs in 2000. Further, these pricing amounts applied to a disproportionately greater number of Medicare beneficiaries. As such, NLAs appeared to constrain more than 98% of Medicare's laboratory spending, making carrier fee schedules and provider charges of minimal relevance to Medicare. Therefore, as noted by the IOM, "in practical terms there is now a *de facto* single fee schedule."⁴ This constrained fee schedule remains largely stagnant, falling behind price increases applying to other elements of health care in the U.S.

An exception to the NLA determination was made in the Benefits Improvement and Protection Act of 2000. Congress approved setting the NLA at 100% of the national median for tests for which the cap was set on or after January 1, 2001.⁶ To date, CMS has applied this provision to 12 diagnostic and screening codes associated with Pap tests.

Fee updates. In 1984, the initial CLFS included a mechanism for annual inflation adjustments consistent with the Consumer Price Index (CPI) for all urban consumers, determined by OMB. However, after a few years, the updates were reduced to a rate less than the CPI or zero, then eventually eliminated altogether.⁴ Following an update in 1997, payment rates for laboratory tests were frozen from 1998 to 2002, and a modest 1.1% inflation update was provided in 2003. The MMA of 2003 cancelled a scheduled 2.6% update for 2006 and enacted another five-year freeze^o for 2004 through 2008.⁶ A longitudinal comparison of the fee updates for laboratory and other services are provided in Table 8.1. This comparison indicates that the 1995-2007 cumulative and average increases for the CLFS were 6.4% and 0.48% as compared to significantly higher increases for all other updates indexes, including 39.4% (2.6%) for CPI-U, 66.3% (4.0%) for CPI-U Medicare, 48.6% (3.1%) for the Medicare inpatient hospital basket, 28.5% (3.2%) for Medicare outpatient hospital care, and 42.3% (2.8%) for the MPFS.

New technologies. For newly developed tests considered to be similar to existing tests, CMS assigns a payment rate based on the rates of the similar existing tests, a process known as "cross-walking."¹² If a test is considered to be a truly novel or breakthrough technology for which there is no existing similar test, CMS relies on carriers to independently set rates for the first year of use. Carriers assign a new code and use data from manufacturers, other carriers, or other information to determine appropriate payment levels for the test along the range of existing payments, a process known as "gap-filling." In turn, CMS sets the NLA for new technologies at 74% of the median rate of all carriers. (This process and corresponding issues are discussed below in the section on coding.)

^o The latest five-year freeze (2004-2008) was established under MMA of 2003 as an alternative to a 20% co-payment requirement for Medicare beneficiaries, whose likelihood of being collected was considered to be low by many laboratories.¹⁰

Negotiated Contracts and Competitive Bidding

Increasingly, federal payers are contracting with private payers (local and regional plans) to offer coverage to their beneficiaries. For example, the Medicare Part C plans (Medicare Advantage) are private sector health plans approved by Medicare to provide Part A and Part B benefits to enrollees who choose this option.^{77,78} Under Part C, Medicare negotiates contracts to make monthly payments to the private plans.⁷⁸ Medicare pays private plans according to the categories under which they fall: local plans or regional plans.

However, in 2006, CMS implemented a system of competitive bidding to set payments for new contracts with preferred provider organizations (PPOs) as required under MMA of 2003. Bids^p made by private plans to offer Part A and Part B coverage to Medicare beneficiaries can directly influence Medicare payment rates. That is, payment rates will be based on the relationship between the private plan's bid rate and the benchmark (which is the county-level payment rates used to pay for Medicare Part C plans before 2006).^q For plans whose standard bid exceeds the benchmark, Medicare's base payment rate is set equal to the benchmark and enrollees are required to pay an additional premium that equals the difference between the bid and the benchmark. For plans whose standard bid is below the benchmark, Medicare's base payment rate is set equal to the standard bid.^r Methodology to determine benchmarks for regional plans is very similar, although CMS uses a more complex formula to calculate the benchmark. (See discussion of competitive bidding further along.)

^p The bid represents the cost to cover an average, or standard, beneficiary; it includes any plan administrative cost and profit.

^q County-level payment rates were at least as high as per capita fee-for-service Medicare spending in each county before 2006 and were often substantially higher.

^r Medicare also pays a rebate to plans that bid below the benchmark, which is defined by law as 75% of the difference between the plan's bid and its case mix-adjusted benchmark. The plan is required to return the rebate to enrollees through supplemental benefits or by charging lower premiums.

**Table 8.1: Medicare pricing updates for certain provider types: percentage changes
1995-2006**

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	Cum.	Avg.
CPI-U (July) ^a	2.8%	3.0%	2.2%	1.7%	2.1%	3.7%	2.7%	1.5%	2.1%	3.0%	3.2%	3.2%	2.5%	39.4%	2.6%
CPI-U Medical Care (July) ^{a,b}	4.4%	3.6%	2.7%	3.4%	3.5%	4.1%	4.5%	4.9%	3.8%	4.5%	4.2%	4.0%	4.3%	66.3%	4.0%
Medicare Inpatient Hospital Mkt. Basket ^c	3.1%	2.4%	2.0%	2.9%	2.5%	3.6%	4.1%	2.9%	2.95%	3.4%	3.3%	3.7%	3.4%	48.6%	3.1%
Outpatient Hospital ^d	Cost-based system - no defined updates					3.6%	4.1%	2.9%	2.95%	3.4%	3.3%	2.2%	3.0%	28.5%	3.2%
Physician Update ^e	7.5%	0.8%	0.6%	2.3%	2.3%	5.5%	4.8%	-4.8%	1.7%	1.5%	1.5%	0.2%	0.0%	42.3%	2.8%
Actual CLFS Update ^f	0.0%	2.9%	2.3%	0.0%	0.0%	0.0%	0.0%	0.0%	1.1%	0.0%	0.0%	0.0%	0.0%	6.4%	0.48%

Sources: ^a For data from 1995 to 2000, *Medicare laboratory payment policy: Now and in the future*. Washington, DC: Institute of Medicine, 2000.

2006 annual update for clinical laboratory fee schedule and laboratory services subject to reasonable charge payment. CMS manual system. Pub. 100-04 Medicare claims processing. Baltimore, MD: Centers for Medicare and Medicaid Services, 2005.

2007 annual update for clinical laboratory fee schedule and laboratory services subject to reasonable charge payment. CMS manual system. Pub. 100-04 Medicare claims processing. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006.

^b Section 1834(h)(4)(A) of the United States Social Security Act. Payment for durable medical equipment.

^c Medicare program; Changes to the hospital outpatient prospective payment system and calendar year 2006 payment rates; Final rule. *Federal Register* 70, no. 217 (November 2005): 69516. Medicare program; Hospital outpatient prospective payment system and CY 2007 payment rates; CY 2007 update to the ambulatory surgical center covered procedures list; Medicare administrative contractors; and reporting hospital quality data for FY 2008 inpatient prospective payment system annual payment update program—HCAHPS survey, SCIP, and mortality. 42 *Code of Federal Regulations*, parts 410, 416, 419, 421, 485, and 488.

^d 2005 annual report of the Boards of Trustees of the Federal hospital Insurance and Federal Supplementary Medical Insurance trust funds. Washington, DC: Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, 2005. ; 2006 annual report of the Boards of Trustees of the Federal hospital Insurance and Federal Supplementary Medical Insurance trust funds. Washington, DC: Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, 2006.

2007 annual report of the Boards of Trustees of the Federal hospital Insurance and Federal Supplementary Medical Insurance trust funds. Washington, DC: Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, 2007.

Consumer price index—All urban consumers. Washington, DC: Bureau of Labor Statistics, 2007.

^e Medicare program; Hospital outpatient prospective payment system and CY 2007 payment rates; CY 2007 update to the ambulatory surgical center covered procedures list; Medicare administrative contractors; and reporting hospital quality data for FY 2008 inpatient prospective payment system annual payment update program—HCAHPS survey, SCIP, and mortality. 42 *Code of Federal Regulations*, parts 410, 416, 419, 421, 485, and 488. Medicare program; Changes to the hospital outpatient prospective payment system and calendar year 2006 payment rates. *Federal Register* 70, no. 217 (November 2005): 68516.

History of the Medicare clinical laboratory fee schedule. Washington, DC: Prepared by Avalere Health for the American Clinical Laboratory Association, 2005.

Medicaid Payment Methodologies

In general, Medicaid payment rates are determined by individual states; however, payment for laboratory services may not be set higher than the Medicare NLA. According to the Kaiser Family Foundation's online Medicaid benefits database, 49 states use a fee-for-service payment methodology to pay for laboratory services and one state (Alabama) uses a reasonable charge methodology.⁷⁹ Specific data indicate that nine states use the NLA as the payment rate, two states use a percentage of the NLA as the payment rate, and other states use some combination of these calculations depending on whether the test is a high or low volume procedure. Eleven states currently require a co-payment for laboratory testing and x-ray services received outside a hospital or clinic.

TRICARE Payment Methodologies

The MHS provides direct care to beneficiaries and allows them to choose an option to receive care from civilian providers. TRICARE Prime is a managed care option, TRICARE Standard (formerly known as CHAMPUS) is a fee-for-service option, and TRICARE Extra is similar to TRICARE Standard but offers discounts when beneficiaries use network providers.^{80, 81} TRICARE has negotiated contracts with approved managed care providers that accept the negotiated rate as payment in full. In 2002, TRICARE issued a request for proposals for new contracts through competitive bid.⁷¹

For laboratory services, TRICARE pays either the rate on the Medicare CLFS or the contract rate negotiated by HMOs and PPOs, whichever is lower.^{s,82} Three regional fiscal intermediaries have been contracted to administer payments for services accrued by TRICARE beneficiaries at non-military health care facilities.⁸³

Payment and contract-related information could not be obtained for the Veterans Health Administration.

Private Sector Payment Methodologies

Private payers often use Medicare's MPFS and CLFS for setting their own payment rates. For example, a payer may pay a multiple or percentage of the rate designated for a CPT or other HCPCS code on the Medicare fee schedule (e.g., multiple of 1.2=120% or 80% of the CLFS). Private insurance companies also may use other methods to determine payment rates, such as a percentage of the laboratory's actual charges (e.g., an 80% payment for a laboratory charge of \$100 for a test) or predetermined rates for services negotiated via contracts with employers or laboratories participating in their network. Private payers also may negotiate rates with employers or participating laboratories, that become contractually binding.³⁹ Unlike Medicare's fee schedule, which is publicly available, data on payment rates and methodologies used by private payers are generally not publicly available.

In addition to Medicare business, private sector payers also negotiate contracts independently with clinical laboratories. Two such contracts were awarded recently. In October 2006, United

^s TRICARE uses an adjustment factor equal to the ratio of the local average charge (standardized for the distribution of clinical laboratory services) to the national average charge for all laboratory services during the base period to establish laboratory service local maximum allowable charges.

Healthcare awarded an exclusive ten-year managed care contract to Laboratory Corporation of America (LabCorp) worth an estimated \$3 billion.⁸⁴ Along with providing laboratory services to United's 28 million members, LabCorp is obligated to develop a series of laboratory networks[†] in selected regions of the country.⁶ The goal of the contract was to cut a minimum of 15% to 20% off United's over \$2 billion per year laboratory testing expenses (including clinical and anatomic pathology outpatient and outreach testing.) Also at that time, Aetna awarded an exclusive contract to Quest Diagnostics. While the financial details of the contracts are not available, a news article quoted laboratory industry professionals who speculated that these contracts provide the insurance companies with testing services at costs that are as much as 45%–55% less than what Medicare pays for the tests.^{85,86}

Outstanding Issues with the Current Payment Systems

The 2000 IOM report, the 2005 report prepared by The Lewin Group, and others have concluded that the Medicare payment policy for clinical laboratory services is outdated and inadequate, and could inhibit beneficiary access and stifle innovation in testing technology.^{4, 10, 87, 88} The IOM Committee on the Medicare's Payment Methodology for Clinical Laboratory Services evaluated the current methodology against five desirable goals of a payment system:

- Beneficiary access to services on a timely basis
- Flexibility to promptly recognize and determine fair payment for new technologies
- Transparency in processes for setting payment policies and amounts that are understandable and open to input from the public and providers
- Value that reflects efficient and appropriate use of laboratory services to support positive health outcomes and quality of care, and eliminate fraud and abuse
- Administrative simplicity and efficiency of the system for the provider, payer, and patient⁴

The IOM committee found significant shortfalls toward all of these goals except beneficiary access. However, other experts, including some in government, assert that access remains limited for screening purposes and nonexistent for predictive purposes.^{35, 47} The IOM committee developed 12 recommendations to begin redesigning the current methodology toward a more rational approach for attaining the five goals. Only one of the recommendations has been implemented since publication of the IOM report in 2000 – improved transparency in the participation of stakeholders in annual meetings of the CMS Council on Technology and Innovation to assess the relationship between current CPT codes on the fee schedule and new testing technologies.⁸⁹

Multiple Fee Schedules Add to Administrative Burden and Result in Payment Inconsistencies

The complexity and inefficiency resulting from use of 56 different fee schedules was cited as a major problem in the 2000 IOM report. The administrative value of the original fee schedule system has been greatly diminished since many of the individual test fees on the schedules are now close to the NLA.⁴ Except for national coverage determinations, the use of different fee

[†] LabCorp will reimburse United Healthcare \$200 million for the first three years of the contract for transition costs related to developing the expanded network in certain local markets.

schedules and corresponding carrier processes for coverage determinations contributes to administrative burden and inefficiencies for all parties involved.

Because the original allowable payments set in 1983 were not linked to laboratories' relative costs associated with performing tests or adjusted for inflation, some fees are most likely low relative to costs while others may be high.¹⁰ Such payment variations are arbitrary, and payment disparities for new tests that are integrated into the existing system often are compounded by other pre-existing variations. For tests where there is not convergence with the NLA (an estimated 25-30% of payments), wide variations in rates among carriers add to the challenges of setting appropriate payment levels.⁹⁰ Variations in 2007 fee schedule payments for the top 15 clinical laboratory procedures (by allowable charges) are listed in Table 8.2. Payment variations are as high as 40% for complete blood count and white blood cell count tests and 54% for a urine culture.⁹⁰

Based on principles of inherent reasonableness, Congress^u gave CMS the authority to modify payment levels for Part B services it considered grossly inappropriate (excessive or deficient) by as much as 15% annually without using public notice and comment procedures.¹⁰ To date, CMS has not employed this authority. The authority notwithstanding, this method of payment adjustment may be impractical, especially as the number of laboratory tests on the market continues to increase.

^u CMS was given this authority under the Balanced Budget Act of 1997.

Table 8.2: Variations across the Medicare Carrier Fee Schedules for the Top 15 Laboratory Tests Ranked by Allowable Charges 2006

Ranked by Total Allowed Charges in 2006	HCPCS Code	Short Description	NLA	2006 Mid-Point	Minimum	Maximum	\$ Difference	% Difference
1	85025	Complete CBC w/auto diff WBC	\$10.86	\$14.68	\$6.50	\$10.86	\$4.36	40%
2	84443	Assay thyroid stimulating hormone	\$23.47	\$31.72	\$21.98	\$23.47	\$1.49	6%
3	80061	Lipid panel	\$0.00	\$0.00	\$13.69	\$18.72	\$5.03	27%
4	80053	Comprehensive metabolic panel	\$14.77	\$19.96	\$11.74	\$14.77	\$3.03	21%
5	36415	Routine venipuncture	\$0.00	\$3.00	\$3.00	\$3.00	\$0.00	0%
6	83036	Glycosylated hemoglobin test	\$13.56	\$18.33	\$9.77	\$13.56	\$3.79	28%
7	83970	Assay of parathormone	\$57.67	\$77.93	\$57.67	\$57.67	\$0.00	0%
8	85610	Prothrombin time	\$5.49	\$7.42	\$4.44	\$5.49	\$1.05	19%
9	80048	Basic metabolic panel	\$11.83	\$15.98	\$8.93	\$11.83	\$2.90	25%
10	84153	Assay of PSA, total	\$25.70	\$34.73	\$20.28	\$25.70	\$5.42	21%
11	82728	Assay of ferritin	\$19.03	\$25.72	\$12.22	\$19.03	\$6.81	36%
12	G0103	PSA screening	\$25.70	\$34.73	\$20.28	\$25.70	\$5.42	21%
13	87086	Urine culture/colony count	\$11.28	\$15.24	\$5.24	\$11.28	\$6.04	54%
14	82607	Vitamin B-12	\$21.06	\$28.46	\$14.56	\$21.06	\$6.50	31%
15	83550	Iron binding test	\$12.21	\$16.50	\$7.58	\$12.21	\$4.63	38%

Source: List of top 100 lab procedures by carrier in descending order by allowed charges. From the 2006 BESS procedure data completed year. Baltimore, MD: Centers for Medicare and Medicaid Services, 2007.

Clinical diagnostic laboratory fee schedule, 2006. Baltimore, MD: Centers for Medicare and Medicaid Services, 2007. History of the clinical laboratory fee schedule. Washington DC: Prepared by Avalere Health for American Clinical Laboratory Association, 2005.

Insufficient Research on Alternatives to the CLFS

In 2000, the IOM committee recommended replacement of the CLFS with a single national fee schedule based on a methodology similar to that of the MPFS. The building blocks for this system would be a relative value scale; adjustments for laboratory, beneficiary, or other characteristics, including geographic location; a dollar conversion factor; and periodic updates. On an interim basis, relative value payments could be calculated using the current NLA.⁴ This would provide time for more rigorous cost-based analyses of alternative methods for gathering data to be used in the calculation of the relative values. The committee identified four approaches worthy of further study by CMS:

- Microcosting studies to determine costs of individual procedures in order to set both the relative value and the conversion factor
- Competitive bidding demonstration project to set the relative value (but not the conversion factor)
- Negotiated fee demonstration project to set both the relative value and the conversion factor
- Analysis of charges to set the relative value (but not the conversion factor)⁹¹

Among these approaches, negotiated rulemaking has proven to be a successful model for updating the physician and ambulance fee schedules.¹⁰ Each alternative offers certain advantages and disadvantages and may have varied implications for the laboratory medicine sector. Since publication of the IOM report, one study of a charge-based relative value payment system has been completed and plans for the competitive bidding demonstration project are underway (following a three-year negotiation of terms with stakeholders). Both of these studies are discussed in greater detail below.

Even though some of the proposed studies have not been completed, many stakeholders contend that an entirely new methodology is needed rather than conversion of the current system to one based on relative value. Among potential alternative approaches are payment based on evidence, test complexity, episodes of care, and cost-effectiveness.

Study of charge-based relative value

In 2002, CMS funded a preliminary study that examined the use of charge data to determine relative values of laboratory tests and compared payment levels across several hypothetical fee schedules in selected carrier markets. All charge-based relative values (CBRV) also were compared to NLA-based relative values. Although it was not a systematic effort to evaluate relative values for laboratory tests, this analysis found that payments for many tests would change under a charge-based approach, including some that would increase or decrease dramatically. A large number of outliers resulted from the comparison of charge-based and NLA-based relative values. Calculations of standard deviations indicated that payment for outlier procedures would either decrease by at least 44% or increase by at least 82% (assuming a constant conversion factor) when a CBRV approach was used compared to the NLA approach.⁹¹ Further analysis revealed that low-volume

procedures accounted for a disproportionate share of outliers.^v In addition, the study found that there would be relatively little redistribution across procedure classes. However, at the level of the individual procedure, differences would be significant for certain tests.^{w,91}

Using a CBRV methodology offers advantages. Since it is based on available claims data, it is relatively inexpensive and administratively straightforward. Supporters of this approach contend that the correlation between charge data and costs is valid. In addition, CBRVs provide an automatic and timely methodology for accommodating the need to set payments for new tests and for updating payments on a regular basis.

The CBRV approach has a few weaknesses that would have to be resolved prior to adoption. First, CBRVs would not help to set payment rates for automated test panels, which are currently bundled. In the current system, automated test panels are paid based on the number of tests performed, the rationale being that the marginal cost of performing an additional test is less than the average cost of the set of tests. The methodology used in this study assumed that the charges associated with a test are independent of other tests. If submitted charges also reflect bundling, then the CBRV methodology could be applied, in principle. Second, because there are limited data on relative costs to compare CBRVs, it was not possible to determine whether the CBRVs provide a good measure of the relative costs. The investigators suggested the use of microcosting studies for this purpose. Third, this study did not examine how to set payment rates for new technologies. Further, use of a CBRV methodology would require adequate provisions to control overcharging.

Competitive Bidding Demonstration Project

Another CMS study to assess payment alternatives involves a competitive bidding demonstration. Competitive bidding refers to cost containment mechanisms whereby providers of a service or product submit price bids to a purchaser (e.g., Medicare). Based on predetermined criteria and the proposed bids, the purchaser selects a winner or group of winners that will provide the services or products at a set price for a set period of time. The goal of competitive bidding is to secure a set of prices that reflect the cost of efficient production, including a normal profit.⁴ A core assumption of competitive bidding is that competitors will reveal the minimum price at which a sale is acceptable, obviating the need for extensive data collection. The approach of competitive bidding has provoked significant controversy among stakeholders. While government payers generally have advocated it, providers, patient groups, and other stakeholders have opposed it.

Since the mid-1980s, the Medicare program has attempted to implement competitive bidding demonstrations for payment of clinical laboratory services, health plans (Part C), drugs and biologics (Part B, e.g., for end-stage renal disease), and DMEPOS (Part B).⁹² Only the latter two have been implemented thus far. Laboratory industry and provider opposition to competitive bidding for outpatient clinical laboratory services helped to persuade Congress to halt implementation of any of these demonstrations. Similarly, there were four attempts to conduct competitive bidding demonstrations for Part C services; Congress and the courts intervened and

^v CBRVs for independent laboratories were significantly different than CBRVs calculated for POLs, and the CBRVs for five of the ten CMS regions included in the study differed considerably from the CBRVs calculated for the nation as a whole.

^w Charge-based payment would be at least 33% lower than the NLA-based payment for 15% of procedures, and it would be at least 33% higher than the NLA-based payment for 28% of procedures.⁹¹

the demonstrations were not initiated.⁹³ However, as stated earlier, competitive bidding was implemented in 2006 to set payments rates for new regional PPOs under Part C. In addition, competitive bidding is now used by the Federal Employee Health Benefits program and TRICARE.

CMS is proceeding with the competitive bidding demonstration project for laboratory services. The attractiveness of competitive bidding derives from its potential for substantial savings to the health system. By limiting existing firms' market power, competitive bidding could encourage efficiency, innovation, and lower costs. The competitive bidding demonstration project (1999-2002) for DMEPOS reportedly reduced Medicare payments by \$7.5 million and reduced beneficiary payments by \$1.9 million without a reduction in access (aggregate savings of nearly 20%).^{94,95} Supporters expect substantially higher savings for laboratory services, estimated at \$1.43 billion over the 2007 to 2011 period (if a national competitive bidding program was implemented).⁹⁶

Many experts believe that overpayment for laboratory services originated in the late 1980s, when the fee schedule was established using payment rates provided by clinicians that had marked up the real cost of the test and kept the difference. Thus, current prices on the fee schedule have no substantial relationship to actual costs.⁸⁶ The IOM recommended a demonstration project in competitive bidding to gather information about needs for administrative resources, management at the local level, and impact on beneficiaries and providers.⁴ Congress included a provision in MMA of 2003 authorizing a competitive bidding demonstration project for clinical laboratory services that would otherwise be paid under Medicare Part B fee schedule.⁹⁷ Congress awarded a task order contract in 2004 to initiate the demonstration. The demonstration project may provide a more realistic assessment that can be used to identify those tests that are relatively expensive to produce and those that are inexpensive. In addition, the data could be used to establish an initial set of relative values for a new payment methodology. Whether CMS will use the data to develop a relative value-based payment methodology or as the pricing mechanism outright is unclear.

Along with these strengths, the IOM Committee examined previous assessments of competitive bidding methodology and expert opinion and identified certain weaknesses of this approach when initiated via exclusive contracts. Specifically, competitive bidding initiatives that rely on exclusive or selective contracting allow only those firms submitting winning bids to participate; losing firms are barred from receiving any payment from these contracts during the time of the procurement.⁴ Such arrangements could have significant impact on the financial health of excluded laboratories and the structure of the industry as well as disproportionately disadvantage certain segments of the market.

CMS will include the 358 HCPCS codes that represented approximately 99% of Medicare laboratory testing by volume and payment in the demonstration project. However, in terms of other parameters, the CMS contractor developed a highly exclusive model as outlined in Box 8.3.

Box 8.3: Design of the Competitive Bidding Demonstration Project for Clinical Laboratory Services

- The demonstration project will use two metropolitan statistical areas (MSAs) to define demonstration sites, and cover all tests paid under Medicare except Pap tests, colorectal cancer screening tests, and new tests added to the CLFS during the demonstration.
- Independent, hospital, and physician office laboratories with \$100,000 or more in annual Medicare Part B payments for nonpatient services will be required to participate in the demonstration, though they do not need to bid on coverage of the entire MSA.* Those that do not submit a bid will be barred from receiving any Medicare Part B payments for the duration of the project.
- A laboratory's bids for individual tests will be weighted according to expected demonstration volume and summed to form a single composite bid. The composite bids will be organized from lowest to highest and, along with unspecified criteria, a "pivotal" composite bid will determine the winners and losers.
- CMS will use the pivotal bids to set and freeze payment rates for the three years of the project. Laboratories with a composite bid equal to or lower than the pivotal bid will be winners.
- Laboratories with a composite bid higher than the pivotal bid will be losers, and will be barred from receiving any Medicare Part B payments for laboratory services for three years.
- To ensure quality, CMS will rely on winning laboratories' compliance with CLIA regulations, PT data, and reporting of data on standardized measures of turnaround time, log-in error rates, and physician satisfaction. TAT measures include: (1) total TAT; (2) transport TAT; (3) processing turnaround time; (4) total turnaround time for statim (STAT) testing; (5) reporting TAT for critical values; (6) reporting TAT for public health disease notification. CMS also will review complaints received through a toll-free hotline for the demonstration.

* POLs and hospital outpatient testing are exempt, except where they function as an independent reference laboratory earning Medicare payments of \$100,000 or more per year.

Source: Report to Congress—Initial report on the Medicare Clinical Laboratory Competitive Bidding Demonstration. Baltimore, MD: Centers for Medicare and Medicaid Services, 2006.

According to 1999 data, laboratories derive about 29% of their income from Medicare Part B payments.⁴ Laboratories that are not selected in the competitive bidding process likely would be subject to steep, immediate cuts in revenue for three years. Industry stakeholders contend that, without the ability to offer laboratory services to Medicare beneficiaries, many local area laboratories may have to close their business. Stakeholders have sought to revise the exclusivity provision, allowing all interested CLIA-certified laboratories to continue providing services for Medicare beneficiaries during the demonstration at the amount accepted as the winning bid.⁹⁸⁻¹⁰⁰ As another alternative, stakeholders have suggested that CMS simply indicate the percentage of cost reductions needed for the Medicare program. However, CMS has maintained the initial framework that bars losing laboratories from any Medicare payments.

Several other prominent issues with the current framework have been voiced by stakeholders. In particular, industry representatives have stated that the \$100,000 threshold is insufficient to protect many laboratories that qualify as small businesses, such as those performing low volume, highly complex testing as a reference laboratory or those that grow their business beyond the threshold.⁹⁸⁻¹⁰⁰ For example, if a laboratory earns \$100,000 or less at the time of the initiation of the competitive bid and elects not to participate, that laboratory will be penalized if, at any time during the demonstration, Medicare payments exceed the \$100,000 threshold.¹⁰¹ The penalty is the forfeiture of any further Part B Medicare payments for the remainder of the demonstration.

The demonstrations likely would force approximately 90% of laboratories in the designated areas to participate. Many small laboratories that earn \$1-2 million per year have expressed that they

cannot afford to lose Medicare payments.¹⁰² With more hospital laboratories expanding outreach testing programs, hospitals also are concerned about how the demonstration would affect their financial status. Laboratories that serve as subcontractors or reference laboratories to other laboratories that win the competitive bid also would be affected by the current design.

Supporters of the competitive bidding proposal disagree as to the financial effect on local laboratories. Several contractors (i.e., winners) will be selected in each of the metropolitan statistical areas, but being named a contractor does not guarantee business. Physicians can choose among several laboratories; thus, even the winning laboratories must compete for business. In theory, competition would increase overall quality of laboratory services. Also, if physicians choose to obtain services from multiple laboratories, this may decrease the potential for loss of Medicare market share among the winners.¹⁰³ However, it is not yet known whether these market effects will occur, and loss of market share may be sizable.

The extent to which competitive bidding of laboratory services affects beneficiaries and providers also is unknown. Because the project confines the provider network, beneficiaries may be required to travel long distances to obtain even basic testing, thereby reducing access to necessary services. A small group of winning laboratories may not be able to accommodate all Medicare beneficiaries in every setting in which laboratory services are needed. Such restrictions could have a detrimental impact on continuity of patient care and, perhaps, health outcomes.^{104,105} Potential problems with the current framework could be accentuated in rural areas and for specialized patient populations. In addition, patient preferences and patient satisfaction also were not incorporated into the competitive bidding process or in its standardized measures for reporting on quality.

A laboratory industry stakeholder group, the Clinical Laboratory Coalition, has been seeking legislative action to address the competitive bidding framework. The House Committee on Small Business held a hearing on this matter in July 2007. Shortly thereafter, Representative Nydia M. Velázquez (D-NY) introduced H.R. 3453 (110th Congress), The Community Clinical Laboratory Fairness in Competition Act of 2007. The Senate version of the bill, S.2099, the Protecting Access to Clinical Laboratory Services Act of 2007, was introduced by Senators Ken Salazar (D-CO) and Pat Roberts (R-KS) in September 2007.

Additional Studies Needed

The IOM proposed microcosting studies using standard accounting practices to collect data on direct costs and develop an appropriate basis for determining indirect costs.⁴ Microcosting (also called activity-based costing) attempts to allocate itemized costs by identifying the components of each individual cost.¹⁰⁶ In the context of the clinical laboratory, microcosting determines the total direct labor and supply costs that are required to produce a laboratory test and can serve as the starting point to determine the total cost and ultimately the price of a test.¹⁰⁷ Data acquisition through microcosting studies is critical to the development of a relative value-based payment system, and could contribute to periodic evaluations of payment appropriateness.

For its report, the IOM committee used a very small resource-costing study to gain an understanding of service level costs. However, the study surveyors obtained only general information.⁵⁵ The lack of standard cost accounting systems for the laboratory's costs separate from the hospital and physician's office, and the general reluctance of laboratories to reveal sensitive, proprietary cost information may be challenges to conducting these studies. New

software programs are making such analyses significantly and, as a result, an increasing number of health care organizations, including clinical laboratories, are incorporating microcosting into their overall management strategies.

A major advantage of microcosting is that it avoids or minimizes distortions in product costing resulting from subjective allocations of indirect costs and thus generates useful data on how money is being spent and whether an organization or entity is operating cost-effectively.¹⁰⁸ Findings derived from microcosting studies could provide insight into whether public and private payers are paying appropriate prices for particular laboratory tests and could be used to educate clinicians on the true cost of ordering laboratory tests.^{4, 109} Because of their level of detail and specificity, microcosting studies also allow others to see how well an analysis matches their own situation, even where patterns of care may differ.¹¹⁰ The investment in carefully designed microcosting studies, along with a standardized accounting mechanism, could yield the type of high-quality data needed to redesign the payment methodology.

Reducing Fraud and Abuse

As in other sectors of health care, laboratory medicine is subject to fraud and abuse in areas ranging from defrauding of payers to billing methods that combine legitimate claim information with falsified information.¹¹¹ Examples of common types of fraud in laboratory medicine include billing for services that were not performed, ordered or needed; up-coding;^x unbundling;^y duplicate billing; and falsifying diagnoses.

Several laws and regulations have been applied to reduce fraud and abuse in clinical laboratories. Under the False Claims Act Amendments of 1986 (Public Law 99-562, 100 Statute 3153), any person who knowingly presents or causes to be presented false claims for payment of government funds is subject to a civil penalty between \$5,000 and \$10,000 plus three times the amount of damages sustained by the government because of the act of that person.^{z, 113} This act has been the primary means by which the DHHS OIG and Federal Bureau of Investigation have investigated fraudulent clinical laboratory billing practices.⁶ The Health Care Fraud and Abuse Control Program, established by the Health Insurance Portability and Accountability Act of 1996, is intended to coordinate federal, state, and local law enforcement efforts to prevent and disclose health care fraud and abuse, including in laboratory services.¹¹⁴

The DHHS OIG has been involved in many actions and projects intended to curb clinical laboratory fraud and abuse. For example, Project LabScam was the first nationwide law enforcement project to occur in the medical field and applied to all major independent clinical diagnostic laboratories in the U.S. It arose from information revealed during the investigation that led to the 1992 guilty plea of National Health Laboratory and its agreement to repay \$111 million.¹¹¹ The Hospital Outpatient Laboratory Project has documented hospital laboratory abuses related to test unbundling, double billing of tests, and improper billing of medically unnecessary tests. With input from medical care industries, the OIG has developed model compliance guidelines for laboratories for assisting

^x Up-coding, also referred to as up-charging, is the misuse of standardized codes (i.e., increasing the bill by exaggerating or falsely representing medical conditions and services provided) to obtain higher payment than legally allowed.¹¹²

^y In laboratory medicine, unbundling occurs when a laboratory bills separately for some or all tests that were analyzed simultaneously by a single piece of equipment on a single patient specimen.¹¹¹

^z The False Claims Act does not encompass tax fraud.

development of effective internal controls to detect and prevent fraud, abuse, and waste.¹¹⁵ Among other aspects, the compliance plan includes written standards of conduct, policies, and procedures that address potential fraud, designation of a chief compliance officer, and a hotline or other means by which complaints can be received anonymously.

Government investigations related to clinical laboratory businesses conducted from 1992 to 2006 are estimated to have resulted in penalties exceeding \$1.727 billion.⁶ Monetary penalties imposed as a result of laboratory fraud and abuse represent a fraction of penalties imposed throughout all health care sectors. In 2005, the federal government won or negotiated an estimated \$1.47 billion in settlements and judgments pertaining to health care fraud cases and proceedings.¹¹⁶ In 2006, state Medicaid fraud control units recovered more than \$1.1 billion in court-ordered restitution, fines, civil settlements, and penalties and obtained 1,226 convictions.¹¹⁷ These units recovered \$709 million in 2005.¹¹⁸

Pod or Condo Laboratories

Another type of fraud-and-abuse pertaining to laboratory medicine is physician self-referral, which is addressed by the Stark laws. Enacted under Section 1877 of the Social Security Act, the laws prohibit physicians from referring Medicare patients for certain designated health services to an entity with which the physician or a member of the physician's immediate family has a financial relationship, unless an exception applies.¹¹⁹ When first enacted in 1989, the law applied only to clinical laboratory services; however, in 1993 and 1994, Congress expanded application of the law to 10 other designated health services and financial arrangements involving physicians. In 2003, Congress authorized certain exceptions in which physicians receive non-monetary remuneration that is used solely to send and receive electronic prescription information. Additional clarification and exceptions were defined in the phase III provisions of the law published on August 27, 2007. However, the final rule did not fully address pathology-related self referrals (discussed below).¹²⁰

The potential for clinical laboratory-related fraud and abuse arises from contractual joint ventures that enable non-pathologist physicians and other entities to profit from self-referrals of pathology services.¹²¹ These arrangements are often cited in connection with regulatory changes affecting billing of anatomic pathology services as well as a loophole in how Medicare assigns benefits, which allows an independent contractor physician or non-physician to reassign Medicare billing privileges to a health care entity.^{121, 122} CMS plans to address these issues in a separate rulemaking.

Two types of these referral arrangements have arisen: “pod” or “condo” laboratories and referring physician billing arrangements.¹²³ Pod or condo laboratories are established by a “manager” in a single office space that subdivides each room or cubicle into a separate, fully equipped laboratory. Each “laboratory” is subleased to a physician group practice. The manager hires technologists/scientists and technicians for each laboratory and one pathologist to supervise all laboratory staff. In seeking to be technically in compliance with applicable exceptions to the federal self-referral law, the staff rotate from one laboratory to the next, reviewing each group practice’s slides. Each physician practice group compensates the laboratory at a discounted rate for each slide reviewed, but bill payers for the entire pathology service. In referring physician billing arrangements, a laboratory offers to perform anatomic pathology services for referring physicians and bills such services at a discount; the referring physician then marks up the bill from the laboratory and bills Medicare.

These arrangements can create incentives for physicians involved in these arrangements to order more laboratory tests or to perform biopsies and other anatomic pathology procedures that may not be necessary, leading to increased and inappropriate utilization.¹²⁰ Medical decision-making and the quality of patient care may also be compromised.¹²⁴ The potential profits to the test-ordering physician are far greater than for clinical laboratory services. Pod or condo laboratories also may violate the anti-kickback statute. Until the rulemaking on pathology services is completed, CMS has emphasized that parties involved in shared arrangements in the same building must comply with the in-office ancillary services exception in operation of their business, not just on paper.¹²⁰

The proposed 2007 Physician Fee Schedule released by CMS included a series of proposals to prevent pod or condo laboratories and other contractual joint ventures.¹²⁵ CMS chose to wait to address the issue in its final fee schedule, stating that it needed more time to study the issues involved. The proposed 2008 fee schedule, published in July 2007, included a series of proposals to prevent pod or condo laboratories; however, these proposals differ substantially from those outlined in the previous 2006 proposed rule.¹²⁶ Specifically, the proposed 2007 billing reforms address self-referral and reassignment abuses by strengthening anti-markup restrictions on the technical component of diagnostic services and by creating new anti-markup restrictions on the professional component. Stakeholders are advocating adoption of these proposed rules.¹²⁴

Limitations Based on Volume

Section 1128(b)(6)(A) of the Social Security Act grants the Secretary of DHHS power to exclude from any federal health care program individuals or entities that have submitted bills or requests for payments containing charges for items or services substantially in excess of such individuals' or entities' usual charges for such items or services.¹²⁷ As such, a supplier or provider submitting a claim to Medicare or to a state health care program that contains charges "substantially in excess" of its usual charges may be excluded from participating in these programs.¹²⁸

In 1990, 1997, and 2003, the OIG^{aa} proposed regulations to provide guidance on the Medicare and Medicaid programs' exclusion authority for submitting claims that contain excessive charges.¹²⁹ The 2003 proposed rule stated that individuals and entities (including clinical laboratories) could be excluded from participating in federal health care programs if their charges or costs are more than 120% of their usual charges or costs.^{bb}

Several laboratory medicine organizations opposed the rule proposed by OIG. In June 2007, the OIG announced that it would not proceed with the 2003 proposed rule, basing its decision on public comments and lack of sufficient information required to establish a fixed benchmark for substantially excessive charges or costs that could be applied across the health care sector.¹³⁰ Despite its decision not to issue a final rule, OIG expressed concern about disparities in the amounts charged to Medicare and Medicaid relative to private payers.^{cc}

^{aa} The Secretary has delegated this authority to the OIG.¹²⁷

^{bb} The proposed 2003 rule exempted physicians on the basis that their payment is based on actual costs and is updated annually.¹²⁹

^{cc} In its decision not to promulgate the 2003 proposed rule, the OIG also stated its continued concern about disparities between the amounts charged to Medicare and Medicaid and private payers.¹³⁰

CODING

Standardized coding systems are used to categorize claims for payment for health care services and ensure that they are processed consistently and systematically.¹³¹ Coding systems use alphanumeric nomenclatures to identify particular health conditions, services, or products. The code assigned to a health condition, service, or product is linked to a payment amount reimbursed to providers. For example, under Medicare, codes are linked to fixed payment amounts via fee schedules. The coding systems that apply to laboratory medicine include CPT codes and HCPCS codes for laboratory tests and services and ICD-9-CM codes for diagnoses.¹³²

The CPT-4, published by the AMA, describes the professional services performed by physicians and is widely used as the standard for outpatient and ambulatory care procedural coding and payment. CPT codes fall within the larger national HCPCS, which was designed initially to represent services provided by physicians and non-physicians to Social Security beneficiaries covered by Medicare, currently is used by physicians to report services provided to Medicare and Medicaid patients.^{10,132} In 2004, there were approximately 1,000 clinical laboratory and pathology codes listed in the 80000-89399 CPT-4 code series.¹⁰ The process for updating these coding systems varies by organization. The ICD is a product of the World Health Organization; however, CDC's National Center for Health Statistics in collaboration with other U.S. government agencies has developed a clinical modification (ICD-9-CM) for use in the American health system. It is used to describe illnesses, conditions, and injuries of people seeking medical services in the inpatient departments of hospitals.³⁵ Box 8.4 depicts the main characteristics of these coding systems.

The CMS HCPCS Workgroup comprises representatives of CMS, the state Medicaid agencies, and the Statistical Analysis Durable Medical Equipment Regional Carrier.¹³³ The workgroup is responsible for considering each request for a change to a HCPCS level II national code at regularly scheduled monthly meetings.^{dd}

The CPT Editorial Panel, which consists of 17 members, 11 of whom are physicians nominated by the National Medical Specialty Societies and approved by the AMA Board of Trustees, is responsible for revising, updating, and modifying the CPT codes.^{ee,134} The Editorial Panel is supported by the CPT Advisory Committee, primarily comprising physicians nominated by the national medical specialty societies represented in the AMA House of Delegates. Applications for new CPT codes are reviewed quarterly by the Editorial Panel and must be submitted by a specific date each year. Because CPT coding changes are made effective only once each year for Category I codes and twice per year for Category II and III codes, the review process for CPT coding applications requires at least 8-15 months.¹⁰ Additional delays of 6-28 months can occur if the medical specialty societies and other reviewers do not reach a consensus regarding coding decisions within the appointed timeframe.

The AMA has recently made efforts to increase the transparency of the coding process. In order to provide public stakeholders more time to comment on coding changes, the public release of proposed changes was moved up from the fall to the summer of each year.¹⁰ The AMA also

^{dd} Prior to 2006, the National Panel was responsible for final coding decisions.¹³³

^{ee} The seven other members of the CPT Editorial Panel consist of four physicians nominated from the Blue Cross Blue Shield Association, America's Health Insurance Plans, AHA, and CMS; one performance measures representative, and two members of the CPT Health Care Professionals Advisory Committee (including one at-large member).¹³⁴

established the Pathology Coding Caucus to allow non-physician stakeholders to play a larger role in the development of CPT laboratory and pathology codes and to review code revision proposals.^{ff,35} The group reviews proposed new codes, suggests revisions to existing codes, and develops consensus recommendations.

Box 8.4: Description of Payment Coding Systems

HCPCS

- Developed by HCFA (now CMS)
- Originally designed to represent physician and non-physician services provided to Medicare beneficiaries
- Federal government currently requires physicians to use HCPCS codes to report services provided to Medicare and Medicaid patients

Level I

- Comprises CPT codes
- Used to report hospital visits, surgical procedures, radiological procedures, supervisory services, and other medical services

Level II

- Known as national codes
- Developed by CMS to report medical services that are not covered in CPT

CPT-4

- Published and maintained by the AMA
- System for describing and reporting physician services in an outpatient setting
- Also used for planning outpatient services, benchmarking, assessing quality of patient services

Category I

- Codes for evaluation and management, anesthesia, surgery, radiology, pathology and laboratory, and medicine

Category II

- Supplementary tracking codes for use in performance assessment and QI

Category III

- Temporary codes representing emerging medical technologies, services, procedures not yet approved by FDA and not otherwise covered by CPT codes

Modifiers

- Supplementary codes that can be reported along with Category I codes to report additional information about unusual circumstances under which a procedure was performed
- Meant to support the medical necessity of procedures that otherwise might not qualify for payment

ICD-9-CM

- Based on classification system developed and maintained by WHO
- Clinical modification published by CDC's National Center for Health Statistics
- CMS, private payers require physicians and other medical providers to report ICD-9-CM diagnostic codes on almost all payment claims

Diagnostic Codes

- Represent the reason why a patient is receiving medical care

Supplementary Codes

- Additional information about the patient and/or circumstances surrounding the patient's illness or injury

Source: Smith GI. Basic CPT/HCPCS coding. 2006 Edition. Chicago, IL: American Health Information Management Association, 2006.

^{ff} The Pathology Coding Caucus consists of representatives from the AMA, Advanced Medical Technology Association, American Association for Clinical Chemistry, American Clinical Laboratory Association, ASCP, American Society of Cytopathology, CAP, National Association of Medical Examiners, U.S. and Canadian Academy of Pathology, CLMA, ASM, and American Association of Bioanalysts.³⁵

Inadequate Mechanism for Adding New Tests

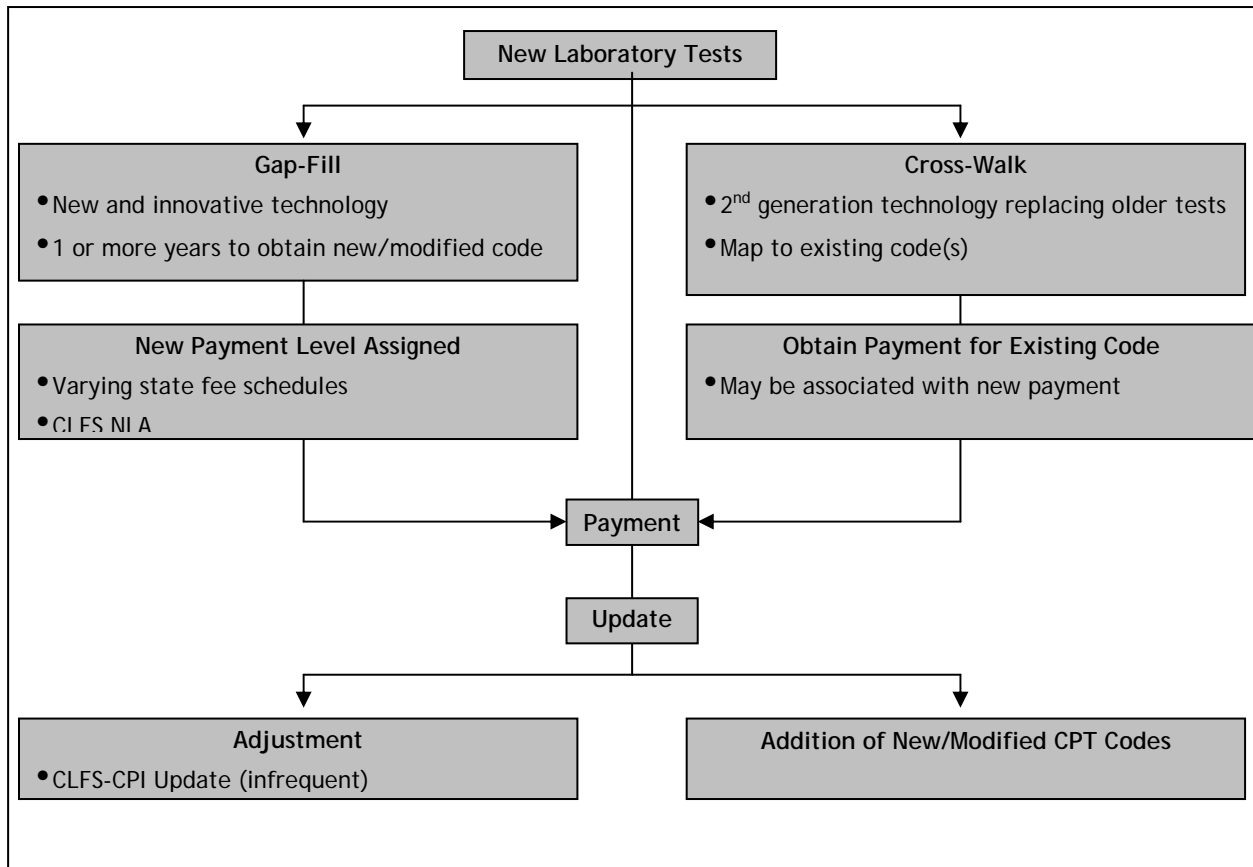
As noted above, CMS incorporates new CPT codes for laboratory tests into the CLFS and establishes payment levels for them using two primary methods: cross-walking and gap filling.¹³⁵ Cross walking is used when a new laboratory test is deemed similar to an existing test, multiple existing test codes, or a portion of a test code that already exists. When a new laboratory test is cross-walked, it is assigned the related existing local fee schedule amounts and resulting NLA. Gap-filling is used when it is determined that a comparable laboratory test does not exist. Under this method, each Medicare carrier is provided with instructions to determine a payment amount for its geographic area(s) to be used for the first year; these carrier-specific amounts are used to establish a NLA for subsequent years. However, gap-filling is rarely used as a payment methodology.¹⁰ Figure 8.1 depicts the basic payment pathways for gap-filling and cross-walking.

The process for updating codes applicable to the CLFS has undergone certain significant changes over the past several years, some of which have been prompted by concerns that the CLFS is not sufficiently subject to stakeholder feedback and that greater opportunity for clinical laboratories and diagnostic manufacturers to provide input would increase the accuracy and efficiency of complex coding determinations.¹⁰ A provision of the Medicare, Medicaid, and State Children’s Health Insurance Program Benefits Improvement and Protection Act of 2000 mandated that the public be given an opportunity to consult on payment determinations for new clinical laboratory tests in a manner similar to the procedures established for implementing coding modifications for ICD-9-CM.⁸⁸ As a result of this and the IOM’s 2001 recommendations, CMS has held a “Laboratory Public Meeting” each year since 2002.¹³⁷ These public meetings, notification of which is given in the *Federal Register*, are intended to allow experts to provide input on the nature of the new test codes and for CMS to receive recommendations regarding cross-walking and gap-filling.

Despite these changes and attempts at greater transparency, the coding system through which new laboratory technologies are added remains inadequate, particularly for new and emerging laboratory tests such as genetic testing. CPT codes used for billing genetic tests identify the test procedure performed (e.g., reverse transcription), but are not specific to the condition being evaluated (unlike codes for most tests which is disease specific).³⁵ Thus, a new genetic test performed with existing procedures receives payment under existing codes, rather than under a newly assigned CPT code and payment rate. (Only novel genetic technologies and testing procedures are assigned a new Category III CPT code.) One of the main criticisms in the use of CPT codes for genetic tests has been the lack of specificity in the codes that limits the ability of payers to make informed claim determinations.

⁸⁸ The ICD-9-CM Coordination and Maintenance Committee, a federal interdepartmental committee co-chaired by CMS and the National Center for Health Statistics, is charged with maintaining and updating the ICD-9-CM system.¹³⁶ Public meetings for discussion or education and proposed coding changes are held by the committee, presenting an opportunity for organizations involved in the coding field, e.g., American Health Information Management Association and AHA, as well as physician specialty groups, to voice their opinions on coding matters. The committee ultimately creates recommendations that must be approved by CMS and the National Center for Health Statistics.

Figure 8.1: Gap-Filling and Cross-Walking Payment Determination Pathways



Adapted from: The Lewin Group. Outlook for medical technology innovation: Will patients get the care they need? Report 2: The Medicare payment process and patient access to technology. Washington, DC: AdvaMed, 2000.

CPT code modifiers have been criticized for being too vague to allow health insurance companies to make well-informed coverage determinations, leading them to deny coverage or request additional information. The Genetic Test Coding Workgroup, a consortium of genetics and laboratory organizations founded by CAP in 2003, proposed a “numeric-alpha” coding section to be added to existing 5-digit CPT laboratory codes used for genetic testing.^{hh,138} The AMA CPT Editorial Board adopted these modifiers, which were included in the 2005 CPT Coding Manual. This coding modification will not change the rates at which these codes are reimbursed.³⁵

Many providers who supply medical services to Medicare beneficiaries argue that payment rates do not correspond to the cost of a genetic test.³⁵ Testimony provided to SACGHS in 2004 indicated that the cost to one academic laboratory in Virginia to perform a genetic test for Fragile X syndrome was \$255, but was reimbursed only \$68 for it. According to this laboratory, major health plans, including both Medicare and Medicaid, reimbursed 60-90% of claims filed for genetic tests.

In its 2006 report on coverage and payment of genetic tests and services, SACGHS recommended that, by 2009, when the freeze on laboratory test payment rates is lifted, DHHS should be ready to revise payment rates to reflect the actual cost of genetic testing.³⁵ SACGHS also recommended

^{hh} This coding system includes a numeral that indicates the disease category and a letter that denotes the gene type, thereby conveying information about the nature of the test being billed.³⁵

that DHHS assess the adequacy of CPT E&M (Category I evaluation and management) codes and allow non-physician health providers deemed qualified to provide genetic counseling services who are currently billing incident to a physician to use the complete range of CPT E&M codes that apply to genetic counseling.

Need for a Better Coding System

Some organizations have advocated the replacement of HCPCS, CPT, and ICD-9-CM with the *ICD 10th revision, Clinical Modification (ICD-10-CM)* and *ICD 10th revision, Procedure Coding System (ICD-10-PCS)*.^{ii,140, 141} In contrast to the ICD-9-CM, the ICD-10-PCS includes a unique code for each substantially different procedure, expandability to allow new procedures to be easily incorporated as unique codes, a multi-axial structure with each code character having the same meaning within a specific procedure section and across procedure sections, and a standardized terminology in which each term has a unique and specific meaning. MMA 2003 includes language that encouraged the Secretary of DHHS to proceed with developing and promulgating rules to adopt ICD-10-CM and ICD-10-PCS.¹⁴²

The transition to ICD-10-CM and ICD-10-PCS has been supported by the federal government and prominent national health care organizations (e.g., AHA, Federation of American Hospitals, and American Health Information Management Association).¹⁴³ A 2005 study by the RAND Corporation estimated that the conversion would cost \$425 million to \$1,150 million in one-time costs, in addition to between \$5 million and \$40 million per year in lost coder and physician productivity over 10 years following conversion.¹⁴⁴ Nevertheless, RAND concluded that the potential benefits of conversion outweighed costs. One of the major benefits of conversion to ICD-10 would be its ability to more finely differentiate between new and old procedures, allowing the value and applicability of new procedures to be more fully realized. Concerns about the high cost of implementation, the magnitude of benefits, and other issues associated with implementation have slowed the transition from ICD-9-CM to ICD-10 CM and PCS in the U.S.¹³⁹

The current coding system also is inadequate for supporting and enabling implementation of HIT. A coding system that provides more accurate, detailed clinical information capable of supporting quality measurement and patient safety efforts will enable a smoother, more effective transition to EHRs and other electronic storage and transfer of health information. Widespread adoption of EHRs and interoperable information networks depends on classification systems that can summarize and report data.¹⁴² The capacity to integrate standardized laboratory data into next-generation clinical practice applications is critical to establishing a national health information network. For example, according to some HIT experts, U.S. efforts to invest in and promote use of SNOMED-CT, a comprehensive, multilingual clinical health care terminology developed jointly by the National Health Service in England and CAP, will be undermined if the U.S. fails to adopt ICD-10-CM and ICD-10-PCS.^{142, 145} The Health Information Technology Promotion Act of 2006 (H.R. 4157), passed by the House in July 2006 but not signed into law, called for the implementation of the ICD-10 coding system by October 2009.¹⁴⁶

ⁱⁱ ICD-10 has been used for mortality classification in the U.S. since 1999 and by health systems in much of the world since the mid-1990s.¹³⁹

CONCLUSIONS

The design and updating of coverage, coding, and payment systems should strive to enable patient access to medically necessary care, support delivery of high-quality care, and sustains innovation of new technologies. Further, they should discourage inefficiency, fraud and abuse, and non-competitive practices. However, these systems can pose significant barriers to achieving these ends in laboratory testing. Changing demographics and disease patterns in the population, corresponding increases in utilization and expenditures, and attributes of emerging technologies are intensifying the challenges to the current laboratory services payment system.

Medicare is the single largest payer in the country, accounting for 29% of all revenues for laboratory services. All public payers and approximately 67% of private payers use Medicare's payment methodologies as the basis for their own and as a tool for negotiating discounts with providers. As such, suboptimal practices and other shortcomings in the Medicare reimbursement system pertaining to laboratory testing affect other public and private sector payers in the U.S. health system.

Key reimbursement challenges to laboratory medicine include the following:

- Medicare's statutory restriction of coverage for screening tests and related preventive services remains a shortcoming in the scope of benefits for Medicare beneficiaries. Adding preventive services to Medicare benefits on a case-by-case basis via the legislative route is cumbersome and impedes access to certain proven, beneficial tests. Legislation is needed that would expand Medicare benefits to include such preventive services that are evidence-based and determined to be reasonable and necessary for prevention and detection of illness or disability among Medicare beneficiaries.
- Continued use of 56 different fee schedules is inefficient and unnecessarily complex. For certain commonly ordered tests, the multiple schedules result in large regional variations, while for other tests, NLAs constrain Medicare payment rate variations.
- There is a notable lack of reliable data on the relationships among historical costs on which the CLFS is based, current production costs, and the effects of economies of scale and other cost-reducing effects of technological changes.
- Studies of data-derived methods for evaluating the appropriateness of payment rates and for designing of potential new payment systems, such as resource-based relative value, microcosting, and negotiated rulemaking, have not been completed.
- CMS is proceeding with a competitive bidding demonstration project for laboratory services, with the expectation of substantial savings. Supporters of the project believe that current prices on the fee schedule have no substantial relationship to actual costs; thus competitive bidding may provide information about resources and costs. However, the project model is highly exclusive and could have significant, detrimental effect on clinical laboratories that loose in the bidding process since many depend on Medicare reimbursement for a sizable portion of their revenues.
- Despite modest improvements in the transparency, processes for establishing payment levels for new laboratory tests, including assignment of new and existing CPT codes to tests and related methods of cross-walking and gap-filling, remain archaic and

inadequate. The expansion of genetic testing, including new types of testing technology and the use of PGx that links tests to therapies, are placing greater strains on flaws in these payment processes.

- From 1992 to 2006, federal government investigations of clinical laboratory-related fraud and abuse resulted in penalties exceeding \$1.727 billion. Current government efforts aim to control fraud and abuse arising from contractual joint ventures that enable non-pathologist physicians and other entities to profit from self-referrals of pathology services. CMS plans to address these issues in a separate rulemaking.
- Redesign of the current Medicare payment system for laboratory services is needed in order to meet the growing scientific, technical, clinical, and economic challenges of the U.S. health care system.

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APPENDIX A

DESIRABLE CHARACTERISTICS FOR PERFORMANCE MEASURE SELECTION CONSIDERED BY IOM, AHRQ, AND OTHER SELECTED GROUPS

To be selected, the measure should rate highly for:

Importance: Is the measure important in a clinical sense, important to the general population, or important to improve the quality of health care delivery.

- The health problem addressed by a measure should be a leading cause of death or disability or associated with high resource use.
- A measure must have an impact on health, be tied to national goals, and be susceptible to being influenced by the health care delivery system.
- A measure should be stratified by race, sex, and age.

Scientifically Sound: This criterion concerns properties of the measure that give it credibility in terms of reliability, validity, and explicitness of the evidence base.

- Reliability means a measure consistently produces the same result when repeated within the same population and setting.
- Validity addresses the question of whether a measure reflects what it is intended to measure.
- The evidence base from which a measure is derived must be explicit—for example, randomized controlled trials, case control studies, observational studies, or formal consensus processes.

Usability: The measure should have been effectively used in the past and have high potential for working well with other measures currently in use. This criterion assesses whether the measure provides a workable solution for the needs of the health care organization.

Feasibility: This criterion refers to the feasibility of implementing the selected measures by examining the existence of measure prototypes, availability of required data across the system, cost or burden of measurement on providers, and capacity of data and measures to support subgroup analyses.

- Existence of prototypes means that the measure has already been precisely defined, field tested, and applied in a variety of settings, such that it can be used by others in a national data set.
- Data required for the measure should be available across the health system for the nation as a whole. The data can be readily collected in the scale and time frame required.
- Cost of measurement should be justified and should not impose an excessive burden on the health system or national collection systems.

- The measure should support meaningful comparisons across subgroups based on population and by health condition.

Alignment: Optimally, measures should be selected from existing leading measure sets that are calculated with the same technical specifications for both the numerator and denominator to reduce redundancy and the burden of reporting.

Comprehensiveness: Measures selected should be part of a set to reflect quality in a particular area of care or bundled services of necessary care for a given condition.

- Each measure in the set should meet the criterion of importance to warrant inclusion.
- To demonstrate comprehensiveness, the set of measures must address the way the care is delivered and the nature of the quality problem involved – underuse, misuse, or overuse.¹⁻⁵

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APPENDIX B

COLLEGE OF AMERICAN PATHOLOGISTS QUALITY INDICATORS FOR PERFORMANCE MEASUREMENT STUDIED IN THE Q-TRACKS PROGRAM AND POSSIBLE ADDITIONAL INDICATORS STUDIES IN THE Q-PROBES STUDIES AND OTHER LITERATURE

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Structural Measures		
Policies, Procedures, and Practices	Not studied or developed.	Laboratories with written guidelines for changing solution in tissue processors and water baths Use or nonuse of preprinted “check off” test order forms Laboratory policies on double checking test orders Implementation of strategies for reducing identification errors <ul style="list-style-type: none"> • Reorganization of phlebotomy • Introduction of electronic event reporting system • Activation of automated processing system Implementation of strategies for reducing errors in surgical pathology <ul style="list-style-type: none"> • Use of checklists • Information access • Use of computerized forms • Use of specific QC processes at each step • Use of standardized tasks and language in reports • Techniques to simplify processes and reduce handoffs • Use of secondary checks • Adjustments in work schedule and environment • Adequacy of staff training • Correct staff for correct job. How often test directory is updated Percentage of tests performed on site (could be POCT) Percentage of tests that must be referred to another laboratory
Staff	Not studied or developed.	Staffing benchmarks <ul style="list-style-type: none"> • Output (workload) per technical staff • Management span of control ratios <ul style="list-style-type: none"> ▪ Measurement of benchmarks in 4 areas: anatomic pathology; chemistry/hematology/ immunology; microbiology; transfusion medicine Percentage of employees complying with universal precautions requirements Number or percentage of employee exposures to bloodborne pathogens

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Access	Not studied or developed.	Percentage of time laboratory hours of operation meet or exceed those of the managed care organization Percentage of time patient waits less than 10 minutes for specimen collection
Technology	Not studied or developed.	Use of Web-based systems for reporting, analyzing, and storing errors Implementation of specifications and strategies to prevent errors in point-of-care testing and measurement of compliance rate <ul style="list-style-type: none"> • Operator certification and validation in POCT (%) • Implement security, validation, performance, and emergency systems existing and new devices • Require flexible user-defined error-prevention system options on instruments as prerequisite for federal licensing • Integrate connectivity standards for data exchange • Preserve fast TATs • Monitor invalid use, operator competence, quality compliance, and other indicators Percentage of laboratory reports reported by each of the following: Fax, phone, computer
Process Measures		
Preanalytic Phase- Clinical and Anatomic Pathology		
Physician Test Knowledge	Not studied or developed.	Not studied or developed. Current substitution: Scope of care within knowledge base (%)
Appropriateness of Test Selection	Not studied or developed.	Measures not developed to evaluate appropriateness of test orders. Current substitution: Testing rates from National Healthcare Quality Report and HEDIS measures, other condition-related measures.
Physician Test Ordering	Not studied or developed.	<ul style="list-style-type: none"> • Requisition slip accuracy and completeness <ul style="list-style-type: none"> ▪ Breakdown of deficiencies by type • Duplicate orders (%)
Patient Preparation	Not studied or developed.	Not studied or developed.
Patient Identification	<ul style="list-style-type: none"> • Wristband error rate (%) • Breakdown of wristband error types (%) 	<ul style="list-style-type: none"> • Patient identification errors caught before reporting (%) • Patient identification errors caught after reporting (%)

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Specimen Labeling/ Identification	Not studied or developed.	<p>Blood bank safety</p> <ul style="list-style-type: none"> • Rate of ABO specimen labeling errors • Rate of ABO typing result discrepancies <p>Specimen labeling</p> <ul style="list-style-type: none"> • Specimens with a labeling error for one or more reasons (%) • Relabeled specimens due to label misalignment (%) • Breakdown of labeling errors by type (%) • Specimen/requisition identification mismatch (%) • Unlabeled specimen (%) • Mislabeled specimen (%)
Specimen Collection	<p>Blood culture contamination rate</p> <ul style="list-style-type: none"> • Total contamination rate (%) • Neonatal contamination rate (%) • Other contamination rate (%) <p>General specimen acceptability</p> <ul style="list-style-type: none"> • Specimen rejection rate (%) • Breakdown of rejection reasons (%) 	<p>Chemistry specimen quality and acceptability</p> <ul style="list-style-type: none"> • Median rates of acceptance • Median rates of rejection due to: <ul style="list-style-type: none"> ▪ Clotted specimen ▪ Container leaking ▪ Specimen contamination ▪ Hemolyzed specimen ▪ Insufficient volume ▪ Tube over/underfilled ▪ Specimen lost/not received ▪ Improper container <p>Hematology specimen quality and acceptability</p> <ul style="list-style-type: none"> • Percentage of submitted specimens rejected for testing • Rate of rejection due to: <ul style="list-style-type: none"> ▪ Specimen damaged in transit ▪ Hemolyzed specimen ▪ Clotted specimen ▪ Specimen delayed in delivery/too old ▪ Insufficient specimen quantity ▪ Specimen contaminated by intravenous solution <p>Phlebotomy</p> <ul style="list-style-type: none"> • Percentage of successful encounters • Percentage of unsuitable specimens • Reasons for unsuccessful encounters (%) <p>Compliance rate (%) with phlebotomy safety practices:</p> <ul style="list-style-type: none"> • Preventing recapping of needles • Discarding tourniquets when contaminated with blood • Glove replacement for each patients • Handwashing between patients

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
		Extraneous tissue in surgical pathology <ul style="list-style-type: none"> • Overall extraneous tissues contamination rate (%) • Location of contamination on slides (% of total) • Origin of contamination (% of total) Specimen adequacy for atypical epithelial cells <ul style="list-style-type: none"> • Median rate of unsatisfactory specimen (%) • Median rate of satisfactory specimen but limited use (%) • Median rate of 3 most common reasons for inadequacy or limited use (%)
Specimen Delivery	Not studied or developed.	Not studied or developed. Current substitute: Delivery within specified time and under specified conditions according to specimen type Courier service <ul style="list-style-type: none"> • Percentage of time courier service picks up specimens on time
Clinical Pathology Specimen Processing and Preparation	Outpatient order entry <ul style="list-style-type: none"> • Outpatient order entry rate (%) • Order entry error rates by category (%) Transfusion blood product wastage <ul style="list-style-type: none"> • Overall wastage rate (%) • Other blood components wastage rates (%) • Breakdown of wastage reasons (%) 	Order entry/transcription error rate Not studied or developed.
Anatomic Pathology Specimen Accessioning and Preparation (Gross Room)	Not studied or developed.	Cutting errors <ul style="list-style-type: none"> • Error rates at tissue, block, slide level (%) • Lack of or incomplete sampling (%) • Injuries to laboratorians (%) Clinical information for surgical pathology <ul style="list-style-type: none"> • Percentage of cases requiring additional information Type of additional information needed (%)
Analytic Phase- Clinical Pathology		
Specimen Analysis	Not studied or developed.	PT specifications and indicators <ul style="list-style-type: none"> • Laboratory tests reported in or out of range (reported by analyte, diagnosis, age group) (%) • QC reported in or out of range (%) Percentage of PT results reported accurately
Report Review or Verification	Not studied or developed.	Percentage of test repeats due to abnormal values or errors identified through autoverification <ul style="list-style-type: none"> • Internal consistency checks • Delta checks

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Analytic Phase- Anatomic Pathology		
Microscopic Specimen Examination	Not studied or developed.	Cognitive and interpretive skills <ul style="list-style-type: none"> • Visual pattern recognition of cells and structures • Development of hypotheses and differential diagnoses • Skill at clinical and histologic grading
Results Review	Gynecologic cytology outcomes-biopsy correlation <ul style="list-style-type: none"> • Predictive value of a positive cytology (%) • Sensitivity (%) • Screening/interpretation sensitivity (%) • Sampling sensitivity (%) • Percent positive for atypical squamous cells of undetermined significance interpretations • Percent positive for atypical squamous cells - cannot exclude high grade squamous intraepithelial Lesions Interpretations • Percent positive for atypical glandular cells interpretations 	Mammographically directed biopsies <ul style="list-style-type: none"> • Correlation of mammographic abnormality with microscopic findings False-negative rate False-positive rate Gynecologic cytology specimen adequacy <ul style="list-style-type: none"> • Mean and median rates of specimen accessioning (e.g., percentage with at least 300 squamous cells and a cluster of endocervical or metaplastic cells) • Mean and median rates of specimen rejection • Mean and median rates of reasons for specimen rejection
Postanalytic Phase- Clinical and Anatomic Pathology		
Turnaround Time and Notification of Critical Values	Stat TAT (outliers) <ul style="list-style-type: none"> • Stat TAT outlier rate (%) • Breakdown of outliers by shift (%) • Breakdown of outliers by day of week (%) TAT for troponin <ul style="list-style-type: none"> • Median TAT of troponin from order to ED availability • Results reported by deadline (%) 	Physician notification of critical values <ul style="list-style-type: none"> • Calls with read-backs (%) • Occurrences where only one call was needed to notify a caregiver of the critical result (%) • Measures of TAT for the following: <ul style="list-style-type: none"> ▪ From result verification to non-physician caregiver notification ▪ From non-physician caregiver notification to physician notification ▪ From result verification to physician notification TAT for surgical pathology reports <ul style="list-style-type: none"> • Median TATs for routine processing • Median TATs for complex cases • Median TATs for processing special-handling cases • Percentage of outliers • Percentage of reports completed within 2 working days • Comparison of surgeon satisfaction and outlier rate • Percentage of presurgical TAT met

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Report Accuracy and Completeness	Test result correction rate	<p>Surgical pathology report accuracy</p> <ul style="list-style-type: none"> • Accuracy/completeness of descriptor analysis for carcinomas that includes <ul style="list-style-type: none"> ▪ Gross measurement of primary tumor ▪ Gross tumor configuration ▪ Histologic type ▪ Histologic grade ▪ Depth of invasion ▪ Margin status ▪ Total number of positive/negative lymph nodes • Documentation errors <ul style="list-style-type: none"> ▪ Transcription error (%) ▪ Documentation error (%) ▪ Poor or incomplete descriptions <p>Practices associated with surgical pathology report completeness</p> <ul style="list-style-type: none"> • Use of standard report form or check list • Amended report rates (%) (clinical pathology) • Aggregate mean rate • Rates according to change in diagnosis, clinically significant information, or patient identification <p>Discrepancies in anatomic pathology reports</p> <ul style="list-style-type: none"> • Frequency of discrepancies by type (e.g., margin status, diagnosis) • Frequency of discrepancies by patient outcome (e.g., no harm, near miss, harm)
Report Delivery	Morning rounds results availability <ul style="list-style-type: none"> • Morning rounds reporting compliance rate (%) 	Errors in report delivery (%) <ul style="list-style-type: none"> • Report delivered to wrong physician • Report delivered to wrong location • Report delivered about wrong patient
Physician Follow-up	Not studied or developed.	Percentage of abnormal reports not documented in patient medical record by test type Percentage of follow-up tests needed but not ordered Percentage of reports appropriately interpreted by clinician Laboratory tests that confirm, alter, or add nothing to patient care
Interpretive Consultation	Not studied or developed.	Consultation rate <ul style="list-style-type: none"> • Aggregate consultation rate • Consultation rate by specimen type • Median TAT • Consultation satisfaction rates (%)

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Outcomes Measures		
Customer Satisfaction	Patient satisfaction with outpatient specimen collection <ul style="list-style-type: none"> • Patient satisfaction score • Percentage of patients “more than satisfied” 	Customer satisfaction in anatomic pathology <ul style="list-style-type: none"> • Overall satisfaction score • Aggregate satisfaction score • Percentage of excellent/good ratings • Percentage of below average/poor ratings • Satisfaction scores for 10 aspects of laboratory service^a Percentage of physician complaints per managed care organization Hospital nursing satisfaction with laboratory services <ul style="list-style-type: none"> • Nursing overall satisfaction score • Aggregate satisfaction score • Percentage of very satisfied/usually satisfied ratings • Percentage of rarely/not satisfied ratings • Productivity ratios: <ul style="list-style-type: none"> ▪ laboratory tests per full-time employee and number of telephone calls per full-time employee ▪ Number of complaints per million laboratory tests • Satisfaction scores for 13 aspects of laboratory services (rated 1-5)^b Calls <ul style="list-style-type: none"> • Percentage of laboratories having written guidelines for handling telephone inquiries and dealing with security (e.g., procedures for caller identification or access to results) • Median time to complete a call • Percentage of calls requiring transfer to another person or laboratory section • Percentage of phone calls answered within 2 minutes of ringing • Percentage of requests for information successfully completed in the original phone call Patient satisfaction <ul style="list-style-type: none"> • Percentage of patient complaints per managed care organization

^a The 10 aspects of laboratory services include (1) quality of professional interaction; (2) pathologist responsiveness to problems; (3) diagnostic accuracy; (4) courtesy of secretarial and technical staff; (5) communication of relevant information; (6) notification of significant abnormal results; (7) pathologists’ accessibility for frozen sections; (8) tumor board presentations; (9) teaching conferences and courses; (10) timeliness of reporting.

^b The 13 aspects of laboratory services include: (1) accuracy of test results; (2) stat TAT; (3) accessibility of laboratory management; (4) promptly answered phone calls; (5) abnormal results notification; (6) routine test TAT; (7) ability to answer telephone questions; (8) laboratory management responsiveness; (9) telephone courtesy; (10) laboratory point of care testing support; (11) phlebotomy courtesy toward nursing; (12) phlebotomy courtesy toward patients; (13) phlebotomy responsiveness to service requests

Step of Total Testing Process	Q-Tracks Performance Indicators	Examples of Performance Indicators From Q-Probes and Other Studies
Other Measures		
Cost-related outcomes		<ul style="list-style-type: none"> • Cost per test • Cost per unit of health outcome • Cost per QALY
Reimbursement-related		<ul style="list-style-type: none"> • Percentage of laboratory tests not reimbursed

APPENDIX C

DEVELOPMENT OF THE MEDICARE PAYMENT SYSTEM

The Medicare program was enacted in 1965 to ensure access to medically necessary care for the elderly and disabled so as to diminish their financial liability, especially with regard to catastrophic illness or disability. While the program's initial structure that provides coverage and payment for hospital care (Part A) and ambulatory care (Part B) remains intact, recent developments include options allowing beneficiaries to purchase private insurance (Part C) and an outpatient prescription drug benefit (Part D). Except for catastrophic coverage, there is no "stop-loss" provision limiting a person's financial liability. Therefore, about 90% of seniors also have supplementary coverage (in addition to Medicare) obtained from various sources, including employers, Medigap, Medicare Advantage (Part C), or via dual eligibility for Medicaid.¹

From its inception until the mid-1980s, Medicare paid for inpatient and ambulatory care, including laboratory tests and services in either setting, using a fee-for-service system based on what providers considered to be customary and reasonable charges. Physicians billed Medicare for laboratory services that they performed in their office and for laboratory services that they purchased at a discount from hospital and independent laboratories.² Many physicians routinely marked up the cost of their purchased laboratory services when billing Medicare and other insurers. The rule was changed in 1980 to eliminate mark ups, but enforcement was difficult.

Steep increases in health care spending prompted further attempts to contain costs. The foundation of the current Medicare payment system was established in the Omnibus Deficit Reduction Act of 1984. Methodologies for calculating costs were further modified through major legislative acts, including the Consolidated Omnibus Budget Reconciliation Acts of 1985 and 1986, Balanced Budget Act of 1997, and MMA in 2003. Each of these acts directly affected payment for laboratory tests and services.

- *Omnibus Deficit Reduction Act of 1984*
 - Eliminated reasonable charge as a basis for payment
 - Allowed physicians to bill only for laboratory tests performed in their offices
 - Established a PPS for inpatient care under Part A that provides specific lump sum payments corresponding to particular patient diagnoses (based on diagnosis-related groups)
 - Established regional fee schedules for physician services, laboratory services, and durable medical equipment under Part B
 - Designated 56 geographic regions for price determinations
 - Set fee schedule payments for clinical laboratory services at 60% of prevailing charges for ambulatory care and 62% for outpatient hospital services
 - Required annual adjustment for all fee schedules according to the CPI and wage rates for each geographic area³

- *Consolidated Omnibus Budget Reconciliation Act of 1985*
 - Established payment caps (deemed NLAs) at 115% of the median of all local fee schedule amounts for each service⁴

Note: Congress eliminated payment rate increases in 1988, reduced hospital outpatient rates from 62% to 60%, restricted updates to 2% of CPI each year from 1991 to 1993, and eliminated updates for 1994 and 1995.
- *Balanced Budget Act of 1997*
 - Established more extensive payment provisions for inpatient care
 - Established PPS for hospital outpatient care (e.g., outpatient surgery)
 - Reduced Medicare payment caps for Part B laboratory services to the lowest of the actual charge by the carrier, 74% of the NLA, or 100% for new test without NLA
 - Required reduction of the number of regional carriers processing laboratory claims from 56 to 5, with one carrier designated as a central statistical resource for such claims
 - Required use of negotiated rulemaking to establish national coverage and administrative policies for Part B laboratory services
 - Required independent laboratories to bill hospitals for their services when they serve as reference laboratories
 - Required DHHS to fund an IOM study on Medicare Part B payments for laboratory services
 - Eliminated coinsurance for Part B laboratory services
 - Established Medicare+Choice (Part C) for managed care
 - Expanded coverage of selected laboratory tests for screening and prevention^a
 - Expanded anti-fraud and abuse provisions
 - Ordered competitive bidding demonstration projects for durable medical equipment
 - Eliminated payment rate increases from 1998 through 2003 for laboratory services⁵
- *Medicare Prescription Drug, Improvement, and Modernization Act of 2003*
 - Established the Medicare prescription drug benefit program (Part D)
 - Provided process for recognition and payment of new medical technology under Part A and Part B

^a Subtitle B of the Balanced Budget Act of 1997 cites coverage for certain screening and prevention tests including mammography, Pap smear and pelvic exams, colorectal screening, diabetes self management, bone mass measurements, and vaccines.

- Improved payment for certain screening tests (e.g., for diabetes, cardiovascular disease, mammography)
- Increased Part B deductible to \$110 in 2005; with subsequent updates by the annual percentage increase in Medicare expenditures
- Mandated use of competitive bidding process for durable medical equipment
- Required competitive bidding demonstration projects for clinical laboratory services
- Eliminated Part B laboratory services payment increases for 5 years (2004-2008)⁶

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