March 10, 2018

Seema Verma, MPH, Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
Attn: CMS-1678-FC Mail Stop C4-26-05
7500 Security Boulevard
Baltimore, MD  21244-1850

Re: Request for Information: Revisions to Personnel Regulations, Proficiency Testing Referral, Histocompatibility Regulations and Fee Regulations under the Clinical Laboratory Improvement Amendments of 1988 (CLIA); CMS-3326-NC

Dear Administrator Verma:

The National Society for Histotechnology is pleased to submit comments regarding Revisions to Personnel Regulations in the above referenced Request for Information. The National Society for Histotechnology (NSH) is a non-profit member organization comprised of over 3,000 members, which supports histotechnicians and histotechnologists worldwide through education, collaboration and innovation. NSH is the leading provider of histotechnology education designed to demonstrate continuing competence in an increasingly complex laboratory testing environment.

Histotechnology is the science dealing with the structure of cells and their formation into tissues and organs, and the profession centers on the detection of abnormal pathology and the treatment for the diseases causing abnormalities, such as cancer.

Histotechnology Pre-Examination and Examination processes are Highly Complex and should be under CLIA’S oversight.

When CMS last revisited the CLIA regulations in 1992, it excluded from oversight many pre-analytic processes because they were deemed relatively simple, minimal risk procedures. Because of this, The National Society for Histotechnology (NSH) is compelled to comment on the Histology Laboratory Personnel Requirements in the above referenced Request for Information.

Much has changed in the last 25 years, and an educated, well-trained Histotechnician/Histotechnologist is essential to arrive at an accurate diagnosis of anatomic pathology samples. The field of histotechnology has witnessed unprecedented technical advances over the last two decades, including innovative approaches, methodologies and automation in traditional areas (tissue processing, histochemistry) as well as in the fields of immunohistochemistry, molecular diagnostics, and computerized assisted digital analysis: all critical to patient diagnosis and treatment. There have been numerous studies which validate and support the evolution of histotechnology, the critical role well-educated and sufficiently trained...
Histotechnicians/Histotechnologists play in quality patient outcomes, and that it is imperative that histotechnology personnel are adequately trained and are under CLIA’s supervision. [See Appendix A]

From the time a tissue specimen is removed from the patient, each step needs extreme care to assure that future histologic studies performed are accurate. In Tissue Resources for Clinical Use and Marker Studies in Melanoma, the authors state the critical importance of high-quality tissue specimens from patients with melanoma. Patient’s samples are now not only used for diagnosis but are also necessary to determine the molecular signature of the tumor to identify patients who may benefit from targeted therapy.

The Histotechnician’s/Histotechnologist’s advanced clinical training and scientific knowledge of dyes and chemicals and best practices used in the clinical histology laboratory, combined with an understanding of tissue composition, make it possible to distinguish tissue structures and features in order to identify advanced disease from normal tissue. These laboratory professionals also perform immunological and molecular (DNA) techniques to identify predictive biomarkers and separate patient tumors into “responders” and “non-responders” for the corresponding therapeutic agent. This identification aids the clinician in selecting a mode of therapy that increases the probability of the desired patient outcome.

In short, the processing of tissue samples has become highly complex, and with personalized medicine becoming the standard of care, the technical quality of the tissue specimen can directly impact quality patient outcomes. The College of American Pathologists (CAP) recognizes and has documented the importance of processing specimens in its Laboratory Accreditation Program (LAP). The checklist notes that slides must have adequate technical quality to be diagnostically useful. Data from proficiency testing such as NordiQC, indicate that approximately 20 percent of breast cancer slides and 30 percent of general slides were found to be of insufficient quality for diagnostic use. [See Appendix B]

Moreover, the NSH/CAP Quality Improvement Program (HQIP) has associated poor tissue processing to poor routine Hematoxylin & Eosin staining (H&E). This stain is performed on each tissue sample that is received in the pathology laboratory for diagnosis. [See Appendix C]

These laboratory professionals need advanced scientific training to assure precision and accuracy from pre-analytical through post-analytical examination of patient pathology samples that require highly complex processing/testing in the histopathology laboratory.

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6 “Anatomic Pathology Checklist CAP Accreditation Program”, College of American Pathologists (2016) page 17
7 Vyberg et al., Immunohistochemical expression of HER2 in breast cancer: socioeconomic impact of inaccurate tests, BMC Health Services Research (2015) 15:352
With change comes the need for educational routes that align with other clinical laboratory scientists, including a greater number of accredited degree programs, culminating in an Associates/Baccalaureate degree. These programs focus on advanced scientific knowledge, technical skills training, as well as, critical thinking and decision making necessary for national certification. [See Appendix D]

I. Personnel Requirements

A. NURSING DEGREE

The following outlines the Society’s views and positions on CLIA’s Personnel Requirements, including those outlined in the CMS RFI referenced on page one of this letter. This section addresses the issue of a nursing degree being considered equivalent to a bachelor’s degree in biological sciences for the purposes of the education requirements for moderate and high complexity testing personnel under CLIA.

“considering drafting proposals to amend 42 CFR 493.1411 (moderate technical complexity technical consultant), 493.1423 (moderate testing personnel), 493.1489 (high complexity testing personnel) to expressly reflect that policy. [CMS is] also considering whether a nursing degree should be considered as a separate qualifying degree, as opposed to the equivalent of a biological science degree, for the purposes of meeting the educational requirements for moderate and high complexity testing personnel and technical consultants. As such [CMS] is also considering proposing to amend §§493.1411, 493.1423, and 493.1489 to add a nursing degree as a separate qualifying degree to the current list of qualifying degrees for the moderate and high complexity testing personnel and technical consultants.”

CMS states in its RFI that it is seeking comment related to whether, for the purposes of meeting the educational requirements for moderate complexity technical consultants and testing personnel and high complexity testing personnel, §§493.111, 493.1423, and 493.1489 should be amended to: (1) To expressly reflect that a nursing degree is equivalent to a biological science degree; or (2) to add nursing degrees as a separate qualifying degree (as opposed to the equivalent of a biological science degree) to the current list of qualifying degrees. NSH’s response to that is (1) NO, a nursing degree is NOT equivalent to a biological science degree, and (2) nursing degrees should NOT be added to the list of qualifying degrees.

1) Nursing Degree is Not Equivalent to Biological Sciences

NSH is a member association of the American Society for Clinical Pathology (ASCP) Board of Governors (B OG). As CMS is aware from member correspondence via the ASCP Board of Governors, NSH is opposed

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The agency’s policies and proposals as noted in its *Survey & Certification Letter 16-18-CLIA*. NSH does not take issue with a nursing degree, or the role that nursing plays in healthy patient outcomes. However, a nursing degree is not intended to be, or should it be viewed as, equivalent to a degree in biological sciences or any other natural science degree required of laboratory testing professionals to perform moderate and high complexity diagnostic testing services.

In the RFI CMS notes that it currently considers a bachelor’s degree in nursing to be equivalent to a bachelor’s degree in biological sciences for the purposes of the education requirements for moderate and high complexity testing personnel under CLIA. In the RFI, it further states it is:

A Bachelor of Science in Nursing (BSN) is a health services degree focused on nursing and is not designed to prepare the student for a career in laboratory diagnostics. In both scope and depth, the natural science coursework required for a biological sciences degree vastly outweighs the natural science coursework required as part of a nursing degree.

According to College Choice, Duke University is home of the number one rated BSN.¹³ Prerequisites for the Accelerated Bachelor of Science Nursing (ABSN) require 6-8 credits in Anatomy & Physiology, and 3-4 credits in Microbiology. The ABSN curriculum include 4 credits in Pathophysiology. A BSN does not meet the minimum academic biological science required in CFR 42 §493.1489.¹⁴ The equivalency determination of the nursing degree inadequately prepares students to meet the current needs and qualifications necessary to perform high and moderate complexity testing and could have significant repercussions for test quality and compromise patient safety and outcomes.

**B. PHYSICAL SCIENCE and NON-TRADITIONAL DEGREES**

CMS indicated that it is seeking input on what is considered a physical science degree and whether any physical science degree(s) should be considered as educational background(s) appropriate for qualifying to meet the CLIA education requirements at §§493.1405, 493.1411, 493.1423, 493.1443, 493.1449, 493.1461, and 493.1489. We believe that the physical science and non-traditional degrees should be accepted, but only if the degree holder has completed 30 hours of biological and chemical sciences, including courses at an advanced level and must meet the requirements for the respective laboratory national certification. Coursework only in physics, astronomy, geology, and other earth sciences does not qualify as medical/histological laboratory science.

**C. Personnel Competencies and Histotechnology**

CMS states it is seeking comments (including information such as evidence, research, and trends) regarding whether general supervisors with associate’s degrees, should be allowed to perform competency assessment for moderate complexity testing personnel in laboratories that perform both moderate and high complexity testing. NSH believes that it is in the best interest of the patient, that all

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¹³ [https://www.collegechoice.net/rankings/best-undergraduate-nursing-schools/](https://www.collegechoice.net/rankings/best-undergraduate-nursing-schools/)  
¹⁴ *CFR §493.1489 Standard; Testing personnel qualifications state that the equivalency personnel must have education and training equivalent to that specified in paragraph (b)(2)(i) ..... that includes: At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, include either 24 semester hours of medical laboratory technology courses; or 24 semester hours of science courses that include: six semester hours of chemistry, six semester hours of biology; and twelve semester hours of chemistry, biology, or medical laboratory technology in any combination; and have laboratory training that includes either*
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laboratory personnel should have the appropriate education and training, including the Histopathology Laboratory.

NSH believes that a laboratory supervisor with an associate’s degree that includes, or has completed at least 60 semester hours, or equivalent, in the chemical biological, and/or clinical laboratory sciences be allowed to perform competency assessments for testing personnel performing moderate to high complexity testing. However, in anatomic pathology laboratories, according to CLIA 88, the technical supervisor is the pathologist. Further, NSH thinks that the anatomic pathology laboratory technical supervisor requirement should be changed to the managing supervisor of the histopathology lab. The managing supervisor is someone who has mastered the specific competencies required for the effective operation of the histopathology laboratory. In most cases, the laboratory supervisor is already performing competency assessments. Changing the histopathology lab technical supervisor requirement to the managing supervisor will align the histopathology laboratory with the other clinical laboratory disciplines under CLIA 88 requirements.

**Histotechnology Laboratories should be classified as High Complexity and Should be Under CLIA’s Oversight**

CFR §493.25 states that a laboratory must obtain a certificate for tests of high complexity if it performs one or more tests that meet the criteria for tests of high complexity as specified in 493.17.

Review of the CLIA categories of tests by complexity indicates that many tasks and tests performed in the histopathology laboratory are in fact of high complexity (CFR 42 §493.5, CFR 42 §493.17). We argue that many of the functions and tests (outside the scope of patient result interpretation) are not only routinely performed by histologist but are also validated and acted upon by histologists in their day-to-day operational responsibilities. From a medical perspective, accurate diagnosis is directly related to patient outcome and therefore the principle goal in diagnostic histopathology. For example, “tissue grossing” is considered a high complexity task because of the need to understand anatomy. Similarly, the histologist not only needs to understand the anatomy, but also needs to understand the anatomical and histological relationships to insure adequate processing, embedding and microtomy; all processes that require knowledge, judgment and analysis on the part of the histologist [See Appendix D]. Failure in any of these critical tasks, compromises patient care. Many of the “CLIA definitions and regulations” are outdated and based on methods and technology that are over 30 years old. There have been significant advances in science and medicine that have and will continue to transform laboratory medicine. Efforts to reduce healthcare costs have also changed the landscape from a “fee for service model” to an integrated team of health care professionals geared towards patient outcomes using the “Total Test Approach.” It is essential that education and training in medical laboratory sciences keep pace with the transition toward personalized medicine in order to provide high quality, outcome based patient care. Below are some additional examples to support our belief that Histotechnology Laboratories should be classified as High Complexity and should be Under CLIA’s Oversight.

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Routine staining and special diagnostic stains require a knowledge of chemistry and biochemistry to troubleshoot and monitor quality.

According to an article in CAP Today\(^\text{16}\): “the great promise of genomics and actionable cancer biomarkers relies on cancer tissues being handled in the right way so that they are suitable for study.” In fact, for over two decades, peer reviewed literature has strongly suggested the need for more rigorous standards to be applied to histopathological sample collection and analysis. A particular emphasis has been placed on using the “Total Test Approach” in Histopathology encompassing pre-analytical, analytical, and post analytical workflow and methodology. Embracing the Total Test Approach is even more important given the increasing number of companion diagnostic assays being developed and in use. Histopathology is entering the era of molecular pathology. Rigorous conformity to best practices will be required to provide; reliable, reproducible and patient focused results

Immunochemical staining and interpretation used for testing a companion diagnostic associated with drug treatment is highly susceptible to the pre-analytical processing. Without proper technical education, incorrect procedures are used resulting in undesirable patient outcomes. This has been well documented by an International Quality Assurance Organization, NordiQC [See Appendix B]

As defined by current CLIA regulations, histopathology laboratories are not considered moderate or high complexity testing facilities (CFR 42 §493.20, CFR 42 §493.25). Although not designated as moderate to high complexity, histopathology laboratories and staff are still required to meet many if not all of the same requirements under quality systems for non-waived testing (CFR 42 Sub K). In addition, while histopathology laboratories are not required to perform extensive proficiency testing, many histopathology laboratories chose to do this on their own, by performing proficiency testing thru non-government accreditation providers. Despite this, histology personnel are still not considered “testing personal” nor are histopathology laboratories currently considered moderate or high complexity laboratories.

D. Personnel Experience, Training and Skills

Currently in the histopathology lab under CFR 42 §493.1489, “testing personnel” is considered the individual reading and interpreting the slides and issuing a report, e.g. the pathologist. At this time, Histotechnicians and Histotechnologists are not considered testing personnel, but their role is critical and essential in performing and evaluating the assays required to arrive at a valid patient diagnosis. This includes the entire testing sequence: from the time the specimen is received until the patient report is finalized (e.g. “the total test”, from pre-analytical thru post-analytical phases). Many states have implemented their own technical licensure requirements for laboratory personnel. In many instances, laboratories institute policies and procedures that are more stringent than CLIA regulations [See Appendix E]. This is because many view CLIA regulations as the minimum education and training requirements for laboratory personnel. In some states, histology personnel are included in the licensing regulations but in others, they are not included. We feel that this is due to the lack of professional recognition of Histotechnicians and Histotechnologists because they are not considered testing personnel by CLIA.

\(^{16}\) Paxton A. (2016) PD-L1, other targeted therapies await more standardized IHC, \textit{CAP Today}, February 2016
1) Histotechnicians and Histotechnologists should be under CLIA’s oversight!

Histotechnologists and Histotechnicians personnel standards should be under CLIA’s oversight. The practice of histotechnology has evolved as noted on page one of this response with significant advances in clinical diagnostic testing (i.e., molecular assays and companion diagnostics) that require advanced education and training. In fact, the College of American Pathologists accreditation check lists state that the slides must have adequate technical quality to be diagnostically useful (ANP.11734)\(^\text{17}\), and the immunohistochemical stains produced are of acceptable technical quality (ANP 22900)\(^\text{18}\). The Society strongly believes that is the responsibility of the Histotechnicians and Histotechnologists to monitor and review the quality of products and services from the Histopathology Laboratory to provide quality assurance. To do so, appropriately educated, certified technical personnel are required to ensure that the diagnostic assay meets the highest quality standards and to provide the best possible patient outcomes.

2) Histotechnicians and Histotechnologists should be nationally certified as a requirement to demonstrating competence.

The current minimum education requirements for moderate complexity testing personnel are “high school education (or equivalent) and on the job training” (CFR 42 § 493.20). The minimum education requirements for high complexity testing personnel are “education and training equivalent to an associate’s degree in laboratory science, or medical laboratory technology from an accredited institution” (CFR 42 § 493.25). Given the complexity of contemporary histopathology laboratories, we strongly feel that the level of education required in CFR 42 § 492.20 does not adequately provide the education and expertise necessary to provide high quality patient care and outcomes. Several studies have considered the relationship between laboratory test quality and laboratory personnel. These studies,\(^\text{19, 20, 21}\) detailed in Appendix G, lend support to the premise that test quality is influenced by academic education, clinical training and/or work experience, and a competency assessment examination. We wish to highlight one study that found that laboratories employing only certified medical technologists produce significantly more accurate results on proficiency tests than laboratories that employ only non-certified technologists.\(^\text{22}\)

The ASCP Board of Certification Program for Histology is an established program that meets CLIA standards for high complexity testing and is the preferred standard in both licensed and non-licensed states. The US Department of Labor’s Bureau of Labor Statistics reports that job prospects will be best for medical and clinical laboratory technicians and technologists who complete an accredited education program and earn professional certification.\(^\text{23}\) We urge that the CLIA recommendations be amended to include Histotechnicians and Histotechnologists under CLIA’s oversight, and that Histotechnicians and

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\(^{17}\) “Anatomic Pathology Checklist CAP Accreditation Program”, College of American Pathologists (2016) page 17

\(^{18}\) “Anatomic Pathology Checklist CAP Accreditation Program”, College of American Pathologists (2016) page 36


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Histotechnologists are required to pass an accredited certification examination for lab personnel performing pre-examination through post-examination processes in histopathology laboratories.

To prevent the requirement from becoming onerous and to address workforce shortage concerns, NSH proposes that On the Job Trained non-certified technicians with at least 5 years’ experience in a CLIA certified laboratory at the time the new regulations go into effect be given 5 years to continue to work and obtain the required high complexity certification per CFR 42 §493.25. We propose a transition period of five years, where uncertified techs must work under the direct supervision of a certified technician.

In conclusion, we are opposed to the Agency maintaining its equivalent position and are similarly opposed to allowing a nursing degree to be listed as a separately qualifying degree. Instead, CMS should allow individuals who have earned a bachelor’s degree to be considered as having met the degree requirements in §§493.1405, 493.1411, 493.1423, 493.1443, 493.1449, 493.1461, and 493.1489, provided they have completed at least 30 semester hours (or equivalent) of coursework in the biological and chemical sciences pertinent to laboratory medicine. Further we believe CLIA should increase its oversight of histology operations by requiring those facilities or entities that perform histologic processing of anatomic tissues to be classified as CLIA-certified high complexity laboratories, requiring that these procedures be performed in an appropriately accredited CLIA laboratory, and processing performed by laboratory personnel who have passed an accredited certification examination such as either the HT/HTL (ASCP).

NSH appreciates the opportunity to comment on this request for information. If we can be of any assistance please do not hesitate to contact Sharon H. Kneebone, CAE, IOM, Executive Director, at (443) 535-4060 or sharon@nsh.org.

Sincerely,

Diane L. Sterchi, HTL(ASCP)
President

cc: NSH Board of Directors
Appendix A: NSH Response to RFI CMS-3326-NC

Citations 1 - 4
Summary of citations listed on page 2 in the NSH Response to CMS-3326-NC

OBJECTIVES: To analyze the demand for services from the nation's medical laboratories, which is predicted to dramatically increase as our citizens age and millions receive insurance coverage through the Affordable Care Act. METHODS: A systematic review of relevant publications and databases was conducted to assess the current state of the nation's medical laboratory workforce and to examine the impact of population demographics and health reform on workforce development to address the future demand for laboratory services. RESULTS: Building a Laboratory Workforce to Meet the Future, a new report from the American Society for Clinical Pathology (ASCP), provides a comprehensive strategy to address the future workforce needs of the nation's medical laboratories to meet this demand to provide timely, accurate, and safe patient care and to fully realize the benefits of personalized medicine. CONCLUSIONS: The report, from the ASCP Task Force on the Laboratory Professionals Workforce, is a comprehensive review of the myriad of factors affecting recruitment and retention of qualified laboratory professionals and provides a set of thoughtful recommendations outlining a multifaceted approach to bolster the pipeline of potential candidates for the profession as well as leadership in health care.


PURPOSE: To develop a guideline to improve the accuracy of immunohistochemical (IHC) estrogen receptor (ER) and progesterone receptor (PgR) testing in breast cancer and the utility of these receptors as predictive markers. METHODS: The American Society of Clinical Oncology and the College of American Pathologists convened an international Expert Panel that conducted a systematic review and evaluation of the literature in partnership with Cancer Care Ontario and developed recommendations for optimal IHC ER/PgR testing performance. RESULTS: Up to 20% of current IHC determinations of ER and PgR testing worldwide may be inaccurate (false negative or false positive). Most of the issues with testing have occurred because of variation in pre-analytic variables, thresholds for positivity, and interpretation criteria. RECOMMENDATIONS: The Panel recommends that ER and PgR status be determined on all invasive breast cancers and breast cancer recurrences. A testing algorithm that relies on accurate, reproducible assay performance is proposed. Elements to reliably reduce assay variation are specified. It is recommended that ER and PgR assays be considered positive if there are at least 1% positive tumor nuclei in the sample on testing in the presence of expected reactivity of internal (normal epithelial elements) and external controls. The absence of benefit from endocrine therapy for women with ER-negative invasive breast cancers has been confirmed in large overviews of randomized clinical trials.

Advances in computer technology continue to bring new innovations to departments of anatomic pathology. This article briefly reviews the present status of digital optical imaging, and explores the directions that this technology may lead over the next several years. Technical requirements for digital microscopic and gross imaging, and the available options for image archival and retrieval are summarized. The advantages of digital images over conventional photography in the conference room, and the usefulness of digital imaging in the frozen section suite and gross room, as an adjunct to surgical signout and as a resource for training and education, are discussed. An approach to the future construction of digital histologic sections and the computer as microscope is described. The digital technologic applications that are now available as components of the surgical pathologist’s workstation are enumerated. These include laboratory information systems, computerized voice recognition, and on-line or CD-based literature searching, texts and atlases and, in some departments, on-line image databases. The authors suggest that, in addition to these resources that are already available, tomorrow’s surgical pathology workstation will include network-linked digital histologic databases, on-line software for image analysis and 3-D image enhancement, expert systems, and ultimately, advanced pattern recognition capabilities. In conclusion, the authors submit that digital optical imaging is likely to have a significant and positive impact on the future development of anatomic pathology.


(Taylor 2000, Hammond, Hayes et al. 2010, Taylor 2014)
Appendix B: NSH Response to RFI CMS-3326-NC

Citation 6
Vyberg et al., Immunohistochemical expression of HER2 in breast cancer: socioeconomic impact of inaccurate tests, BMC Health Services Research (2015) 15:352
Immunohistochemical expression of HER2 in breast cancer: socioeconomic impact of inaccurate tests

Mogens Vyberg1*, Søren Nielsen1, Rasmus Røge1, Beth Sheppard2, Jim Ranger-Moore2, Eric Walk2, Juliane Gartemann3, Ulrich-Peter Rohr3 and Volker Teichgräber3

Abstract

Background: Treatment for patients with breast cancer (BC) is guided by human epidermal growth factor receptor 2 (HER2) status. The patient’s HER2 status is assessed using US Food and Drug Administration-approved in vitro diagnostic (IVD) immunohistochemical (IHC) tests and laboratory-developed IVD tests. We analysed HER2 testing accuracy using data from the Nordic Immunohistochemistry Quality Control (NordiQC) HER2 IHC programme; results were used in an economic BC treatment model.

Methods: Data were obtained from NordiQC HER2 BC surveys performed from 2008 to 2012. False-negative (FN) and false-positive (FP) rates for approved and laboratory-developed IVDs were used to estimate direct costs, loss of survival, productivity benefit and quality-adjusted life-years. In the absence of consistent and accessible clinical and economic data from countries participating in the NordiQC programme, United States productivity data, healthcare costs and patient numbers were used as a surrogate in order to estimate the potential impact of selecting an approved or laboratory-developed IVDs.

Results: In total, 1703 tests were performed. Pooled FN rates were 11 % for approved IVDs and 25 % for laboratory-developed IVDs; FP rates were 0 % and 5 %, respectively. Using these FP and FN rates in the economic model and applying them to the United States BC population, approved IVD tests would result in better clinical outcomes, i.e., better survival and fewer disease recurrences/progressions, and lower costs, i.e., total direct costs and lost productivity, versus laboratory-developed IVD tests. Every $1 saved by laboratories by using cheaper reagents could potentially result in approximately $6 additional costs to the healthcare system.

Conclusions: The results of this analysis suggest that incorrect HER2 test results have far-reaching clinical and economic consequences.
features and molecular profiles. Correct identification of tumour receptor status (ER/PgR for endocrine therapy and HER2 status for targeted therapy) is a prerequisite for treatment planning. In order to qualify for HER2-targeted therapy, the patient must have a HER2-positive tumour. This can be determined by measuring HER2 protein levels using immunohistochemistry (IHC) and/or by measuring HER2 gene amplification by in situ hybridization (ISH). Current guidelines recommend using either IHC or ISH to assess tumour HER2 status for all patients with breast cancer. Both tests are used, in case an equivocal result is obtained with the first test [3, 10].

The reliability and accuracy of HER2 IHC assays used in clinical practice has improved since the publication and endorsement of procedural guidelines [11, 12]. Many countries now have proficiency programmes for in vitro diagnostic (IVD) HER2 testing to ensure the required accuracy standards are maintained. However, not all IVD test systems perform equally. Performance depends on the quality of assay reagents and the reliability of test protocols. Some IVD tests are available as industrially produced and packaged products that are validated, approved and regulated by the US Food and Drug Administration (FDA). Other IVD tests are created by the pathology laboratories conducting the test, which assemble them from individually available components (often referred to as laboratory-developed tests). When used properly, both the approved and laboratory-developed IVDs can perform equally well; conversely, both classes of IVD have the potential to fail and produce incorrect results. Approximately 67 % of HER2 tests performed by participants in the Nordic Immunohistochemistry Quality Control (NordiQC) programme were approved and validated IVD tests, while the remaining 33 % of tests were laboratory-developed IVD tests (NordiQC 2008–2012). Similar proportions (71 % approved IVD tests and 29 % laboratory-developed IVD tests) have been reported for participants in the UK National External Quality Assessment Service (NEQAS) Breast Screening programme [13]. In some countries, the proportion of tests performed using approved IVD tests may be lower. For example, in a Belgian survey of HER2 testing, only 4 of 34 laboratories used an approved IVD testing kit [14].

The techniques and technologies underlying HER2 testing are not always made clear to oncologists because samples are processed independently in pathology laboratories; however, the oncologist needs a categorical answer regarding the patient's HER2 status. The decision to treat a patient with HER2-targeted therapy is based largely on the reported result of the IVD test, which—if incorrect—may have significant consequences for both the patient and the society.

The aim of this study was to compare the socioeconomic consequences of the accuracy of different HER2 IVD testing procedures using data from a real-world testing/proficiency programme run by the NordiQC group. In this report we describe the reliability of results obtained from approved and laboratory-developed IVD IHC tests assessed by the NordiQC group and consider the potential clinical, economic and socioeconomic impact of inaccurate HER2 test results and subsequent treatment for patients with breast cancer.

Methods
Data sources
HER2 IHC testing data were collected and provided by the NordiQC organisation. These data were used in an economic model of breast cancer that was developed at Ventana Medical Systems, Inc./Roche.

NordiQC programme
Pathology laboratories in over 40 countries that perform IHC tests are invited to participate in a quality assessment of their immunostaining procedures as part of the NordiQC Breast Cancer HER2 IHC programme (Fig. 1). There are two shipments (or runs) per year, each of which contains a 5-core microarray slide of breast cancer cores with varying predefined HER2 expression (0/1+/2+/3+) and amplification levels (both amplified and unamplified for 2+ cancer cores) as verified by using two IHC FDA/CE-IVD approved assays (HercepTest™, Dako, Glostrup, Denmark; PATHWAY®, Ventana Medical Systems, Inc., Tucson, AZ, USA) in NordiQC reference laboratories, and using the HER2 fluorescence in situ hybridisation (FISH) pharmDX™ Kit (Dako). Laboratories use their own standard protocol to stain slides and return them for central assessment by the NordiQC assessor group, which is blinded to laboratory identity and assay used. False negative (FN) and false positive (FP) definitions and values obtained from the NordiQC programme were used. In brief, an FN reaction was defined as a HER2 staining reaction which was scored by the assessors as 0/1+ in a HER2 gene amplified tumour with a 2+/3+ HER2 expression in the reference laboratories. An FP reaction was defined as a HER2 staining reaction which was scored by the assessors as 3+ in a HER2 gene non-amplified tumour with a 0/1+/2+ HER2 expression in the reference laboratories.

Data from the NordiQC website for runs B6–14 were used in this analysis [15].

The study involved the use of data obtained from a quality assurance program based on anonymous human biological material collected in accordance with legislation at the site of collection; as a result, no ethics committee approvals were needed.

Cost calculator/modelling tool
For the approved and laboratory-developed IVD tests, the possible consequences of FP and FN HER2 test
H0648g study by Slamon and colleagues [7]. The number of patients who avoided disease progression because of the lower FN test rate with an approved IVD in comparison with a laboratory-developed IVD test was calculated based on disease-free survival data from the H0648g MBC trial [7].

The number of quality-adjusted life-years (QALYs) lost as a result of a patient not receiving trastuzumab was also calculated. Lost productivity was based on the loss of QALYs, assuming an interaction between QALYs and productivity, both of which are influenced by health state and deteriorate in parallel [17].

A cost calculator was developed to assess the direct financial impact of FN and FP tests. A societal perspective was adopted and US costs were used because of the homogeneity of pricing in the US healthcare system compared with the variety of systems in place in the EU. Costs were adjusted to 2014 values using an annual inflation rate of 3 % [18]. For patients with EBC, a 5-year time horizon was used to generate an annualised 1-year time horizon; a 1-year time horizon was used for patients with MBC.

All results were extrapolated to the estimated numbers of patients receiving systemic treatment for breast cancer in the US to correspond with the use of US economic data and weighted according to the observed prevalence of patients with IHC 0/1+/2+ unamplified carcinomas, 2+ amplified carcinomas and 3+ carcinomas (80 %, 4 % and 16 %, respectively) [19]. This extrapolation was performed to gain an effect of the potential costs associated with selection of the IVD test and was not intended to suggest that such costs might be saved or accrued in the US.

Results

Key features of the NordiQC HER2 testing programme are shown in Fig. 1. Sample test results are shown in Fig. 2, highlighting accurate and inaccurate staining of the samples.

IHC test results

NordiQC HER2 testing data obtained from runs B6 to B14 were pooled [15]. The overall FP rate was 0 % (0 of 1145 samples) for the approved IVD tests and 5 % (28 of 558 samples) for the laboratory-developed IVD tests. FN rates were 11 % (127 of 1145 samples) for the approved IVD tests and 25 % (141 of 558 samples) for the laboratory-developed IVD tests (Table 1).

Impact of inaccurate results on patient outcomes

Calculations for patient outcomes were based on the estimated 232 340 patients with invasive breast cancer in the USA in 2013 [20], 132 433 (57 %) of whom are
estimated to have EBC requiring systemic therapy and 16,263 (7%) of whom have MBC; the remainder have EBC that does not require systemic therapy.

For patients with EBC, an FN HER2 test was calculated to result in a difference of 3.9% per annum in additional life expectancy that might have been achieved if the patient had received trastuzumab, based on cumulative progression over 5 years in 18.2% of patients with EBC [16]. Using the NordiQC FP and FN rates, the estimated loss of survival per patient would be 0.0045 years for the approved IVD tests and 0.0102 years for the laboratory-developed IVD tests. Extrapolation to the US breast cancer population over a 1-year time horizon would give a total missed gain in life expectancy of 177 and 403 years, respectively, for the approved and laboratory-developed IVD tests, representing a difference of 226 years (Fig. 3a). A similar calculation was performed for patients with MBC, based on the 4.8 months' additional life expectancy provided by trastuzumab (median overall survival 25.1 months for chemotherapy + trastuzumab vs 20.3 months for chemotherapy alone) [7]. The estimated total missed gain in life expectancy would be 215 years for the approved IVD tests and 488 years for the laboratory-developed IVD tests, representing a potential difference of 273 years for patients with MBC (Fig. 3a).

The estimated effect of an FN HER2 test on the number of patients with disease recurrence or progression was also calculated. Based on the estimated incidence of disease recurrence in 3.9% of patients with EBC [16], 170 EBC patients tested with an approved IVD HER2 test and 387 tested with a laboratory-developed IVD HER2 test would have recurrent disease as a result of (Fig. 3a). Widespread cytoplasmic reaction is seen in all four tumours. The stain of unamplified tumour c might be interpreted as a 3+; the tumour therefore would not be not reflexed to FISH test and the patient would erroneously be offered trastuzumab treatment.

Table 1  FP and FN rates for immunohistochemical testing as recorded by the NordiQC programme

<table>
<thead>
<tr>
<th>Data source</th>
<th>Approved IVD, n (%) (n = 1145)</th>
<th>Laboratory-developed IVD, n (%) (n = 558)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FN (%)</td>
<td>FP (%)</td>
</tr>
<tr>
<td>NordiQC runs B6–14a</td>
<td>127 (11)</td>
<td>0</td>
</tr>
</tbody>
</table>

FN false negative, FP false positive, IVD in vitro diagnostic, NordiQC Nordic Immunohistochemistry Quality Control Group

*aNordiQC IHC quality-control organisation, B6–14 runs [15]. Laboratories were provided with samples that were IHC 0, 1+, 2+ and 3+
the FN test result. In total, an estimated 217 recurrences in patients with EBC could be avoided annually through the use of approved versus laboratory-developed IVD HER2 tests (Fig. 3b). In patients with MBC, based on an estimated difference in progression-free survival after 1 year of 16% between patients treated with trastuzumab and those who did not receive trastuzumab [7], 86 patients tested with an approved IVD and 195 tested with a laboratory-developed IVD HER2 test would have progressive disease as a result of the FN result. This is the equivalent of 109 progressions in patients with MBC that could be avoided each year by using an approved instead of a laboratory-developed IVD test.

In patients with EBC, false test results would result in a missed gain in QALYs of 0.0038 for patients tested with an approved IVD compared with 0.0086 QALYs for those tested with a laboratory-developed IVD. When extrapolated to the US population, assuming a time horizon of 1 year and weighting according to the prevalence of IHC categories, this led to an estimated 149.7 missed QALYs in patients tested with an approved IVD, vs 342.3 missed QALYs in those tested with a laboratory-developed IVD, a difference of 192.5 missed QALYs in favour of the approved IVD test. In patients with MBC, the corresponding values would be 0.0024 QALYs and 0.0054 QALYs, resulting in a potential difference between approved IVD tests and laboratory-developed IVD tests of 15 QALYs when applied to the US breast cancer population (Fig. 3c).

**Economic cost of inaccurate results**

As shown in Table 2, the estimated total direct cost of an FP or FN HER2 test for a patient with EBC that could be avoided each year by using an approved versus a laboratory-developed IVD HER2 test was $364 for the approved IVD tests and $1394 for the laboratory-developed IVD tests. When extrapolated to the US population with EBC and weighted according to the prevalence of the IHC categories to gain an estimate of the potential effect of use of an approved or a laboratory-developed IVD, this translated into potential total direct costs of $14 447 666 for approved IVD tests and $55 1377 720 for the laboratory-developed IVD tests. Corresponding values for MBC were $859 446 and $5 992 471, respectively (Table 3). Use of an approved
IVD rather than a laboratory-developed IVD test would result in potential savings of $40,930,054 for EBC and $5,133,025 for MBC. Therefore, use of approved rather than laboratory-developed IVD tests could result in a saving of approximately $46 million.

In terms of lost productivity, FN and FP HER2 test results associated with approved versus laboratory-developed IVD tests would result in a reduction in lost productivity estimated at $4,244,968 in patients with EBC, assuming a time horizon of 5 years, annualised to give a 1-year time horizon. In patients with MBC, the difference between approved and laboratory-developed IVD tests would be $330,627.

Despite the more expensive initial outlay for the approved rather than the laboratory-developed IVD tests, the approved IVD tests could still potentially generate considerable savings. Considering a differential cost, in terms of reagents alone, of approximately $35 between the approved and laboratory-developed IVD tests used in the NordiQC laboratories, reagents for the primary testing of US breast cancer patients with an approved IVD could potentially cost approximately $10 million per annum, with a further $15 million associated with total additional direct costs resulting from FN and FP test results could amount to $60 million. The ratio of reagent:direct costs for the laboratory-developed IVDs ($62.5 million) and approved IVDs ($25 million) is therefore estimated at 2.5:1.

**Discussion**

HER2 expression in breast cancer tissue is indicative of an aggressive pathology. HER2 expression is therefore considered a marker of poor prognosis and results from clinical trials have demonstrated a significant benefit for HER2-targeted therapy in patients with HER2-positive EBC [8] and MBC [7]. Therapeutic inhibition of the HER2 pathway has the potential to counteract the prognostic risk associated with HER2 positivity. Currently, four HER2-directed agents are available for use in the treatment of HER2-positive breast cancer: the antibodies trastuzumab, pertuzumab and trastuzumab emtansine, and the tyrosine kinase inhibitor lapatinib. However, the benefit of HER2-targeted therapies is restricted to patients with HER2 gene amplification or protein overexpression. All HER2-directed therapies can cause severe adverse events and have a heightened risk of causing significant patient harm when used in error. Therefore, they must only be administered to eligible patients most likely to respond. HER2-targeting agents are expensive medicines and are only cost-effective if used correctly. Therefore, accurate HER2 testing and HER2 status determination is fundamental to the

### Table 2

<table>
<thead>
<tr>
<th>Outcome, US $</th>
<th>Early stage breast cancer</th>
<th>Laboratory-developed IVD</th>
<th>Difference</th>
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<td>$3,301,263</td>
<td>$7,546,231</td>
<td>$4,244,968</td>
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</table>

**IVD in vitro diagnostic**

aCosts corrected for the prevalence of IHC 2+ tumours [19]. bProductivity loss per year per patient undergoing a HER2 test. cCost for the annual number of new patients undergoing a HER2 test and receiving systemic treatment in the USA

### Table 3

<table>
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<tr>
<th>Outcome, US $</th>
<th>Metastatic breast cancer</th>
<th>Laboratory-developed IVD</th>
<th>Difference</th>
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<tr>
<td>Total cost of lost productivity</td>
<td>$255,594</td>
<td>$586,221</td>
<td>$330,627</td>
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</table>

**IVD in vitro diagnostic**

aCosts corrected for the prevalence of IHC 2+ tumours [19]. bProductivity loss per year per patient undergoing a HER2 test. cCost for the annual number of new patients undergoing a HER2 test and receiving systemic treatment in the USA
success, safety and cost-effectiveness of breast cancer treatment programmes.

Analysis of HER2 status may be requested by oncologists who may have limited knowledge of the reliability and accuracy of the currently available HER2 testing methodologies used in the pathology laboratory. The oncologist must rely on the pathology report as the basis for selecting subsequent therapy for the patient, whose treatment outcome and safety ultimately depend on the result of this test.

Public regulations and controls on the accuracy of HER2 IVD tests are not uniformly available or executed. HER2 immunostaining must be carefully calibrated in order to define with a high degree of reliability which carcinomas are HER2 amplified. The NordiQC quality assessment programme for HER2 is based on a composition of five samples with HER2 expression of 0 to 3+ as defined in reference laboratories. Two of the samples are IHC equivocal (2+), one amplified and one unamplified, the staining reactions of which are particularly important for correct calibration. All laboratories examine the same five highly and robustly characterised tumour specimens using their own standard procedures, providing NordiQC with a good understanding of the quality of their staining procedure. When a HER2-amplified tumour with an expected 2+ IHC reaction is under-stained, giving a 1+ reaction, the tumour will be considered unamplified and not reflexed to FISH. Likewise, when a HER2-unamplified tumour with an expected 2+ IHC reaction is over-stained, giving a 3+ reaction, the tumour will be considered amplified and not reflexed to FISH. Thus, the inclusion of IHC-equivocal tumours is essential to reveal insufficient staining reactions, which may not be identified if only tumours with 0 and 3+ HER2 expression are included, as is the case in other programmes. As there is a degree of flux in participating laboratories and some additional variation in assays used even by long-term participants, there is inevitably some variation in results over time [15]. Nine consecutive runs, B6–B14, were chosen as they were based on the same composition of tumours. Run B6 was the first to include two IHC-ambiguous (2+) cancers, one being amplified and one unamplified; run B14 was the last before the ASCO/CAP guidelines were changed. As a result of the revisions to the guidelines, some tumours previously classified as 1+ are now classified as 2+, which reduced the proportion of FN cases while in-creasing the load of FISH tests. Examination of this series of runs, all of which were performed under consistent conditions and in line with the same guidelines, has allowed us to gain the greatest insight into and most reliable assessment of the quality of HER2 IHC testing among laboratories participating in the NordiQC programme.

In Europe, besides a general quality/safety label for medical devices, no further discrimination of HER2 test systems exists. In the USA, however, the FDA strictly oversees IVD tests that are used for any treatment decisions. For a variety of reasons, not least of which is the high development cost of such an approved test that involves extensive independent validation and proof of clinical utility from clinical trials, few diagnostic tests have been approved by the FDA. Approved IVD tests sell at a higher price than laboratory-developed IVD tests. Many laboratories are urged to be as cost-saving as possible and prefer to run laboratory-developed test systems because of the lower reagent costs involved. Our analysis was undertaken to raise awareness of the potential clinical, economic and socioeconomic differences between FDA-approved and other available assays and to provide oncologists with the information necessary to discuss with pathologists which tests to use for maximum patient benefit and safety. Moreover, it is important to demonstrate to payers that an accurate HER2 result has a greater impact on costs than simply the up-front cost of the test.

To the best of our knowledge, this is the first analysis to calculate FN and FP rates for approved and laboratory-developed IVD tests using ‘real-world’ HER2 results from a proficiency testing programme. Analysis of the NordiQC test programme provided FN and FP rates of 25 % and 5 %, respectively, for the laboratory-developed IVD tests and 11 % and 0 %, respectively, for the approved IVD tests. The large majority of inaccurate test results resulted from the failure to correctly identify IHC 2+ samples. Notably, almost all (83 %) of these incorrect results falsely identified samples as being HER2 negative, which could result in a HER2-positive patient (positivity to be confirmed by reflex ISH to determine HER2 amplification status) not receiving anti-HER2 treatment. Our findings are supported by similar results obtained by the UK NEQAS IHC Breast Screening programme: based on runs 100, 101 and 102, laboratories using approved IVD kits had pass rates of 91 %, 88 % and 94 %, compared with pass rates of 23 %, 47 % and 43 % for laboratory-developed IVD tests [13]. In a German ring study of breast cancer testing procedures, discordant results with a high percentage of FN scorings were encountered in HER2 equivocal (IHC 2+) cases compared with IHC 0/+ and 3+ cases, with only 41 % of participants scoring these cases correctly [21]. This underlines the importance of including 2+ cases in the HER2 challenges.

Based on the economic model, which used US epidemiological and economic data in the absence of consistent, publicly available data for the countries participating in the NordiQC programme, using approved rather than laboratory-developed IVD HER2 tests could result in a
saving of $46 million per year, largely as a consequence of the correct use of trastuzumab leading to avoidance of treatment costs associated with disease recurrence and progression. Although reagent costs are lower for the laboratory-developed IVD tests, the approved IVD tests are still cost saving when a broader perspective is taken, as the overall cost of using a laboratory-developed system is approximately 2.5 times greater than the overall cost of approved IVD tests. For each $1 saved by the pathology laboratory by using cheaper reagents, the healthcare system is potentially burdened with approximately $6 in additional costs. Extrapolation of these results to the EU breast cancer population, where the numbers of patients with EBC and MBC are greater than the numbers used in our analysis, suggests that the potential for savings is even greater, particularly if other HER2-overexpressing cancers are considered [22].

Some potential limitations of this analysis should be considered. The NordiQC programme uses only five tissue samples. If any of these are unusual in a way that affects the performance of approved and laboratory-developed assays differentially, this could have created bias in the comparison. We can think of no plausible mechanism by which such an interaction between sample and assay type could occur, but acknowledge that both the performance characteristics of the various assays, as well as the properties of the samples being tested, may influence the results obtained in a small testing population. In addition, samples that were most often insufficiently stained by participating laboratories are less prevalent in the general population (two of five samples [40 %] in the NordiQC array were IHC 2+, compared with a prevalence of such tumour types in the population of approximately 12 %). We allowed for this by weighting the results accordingly [19]. In addition, our calculations are based on comparing hypothetical situations in which laboratories either all use approved IVD tests or all use laboratory-developed IVD tests, whereas the reality is that a relatively small proportion of participating laboratories use laboratory-developed IVD tests. The proportion using laboratory-developed IVD tests may be significantly higher in laboratories not participating in proficiency programmes, however. Finally, this analysis was based on an economic analysis with the assumptions and estimations inherent in such models. Our intention was to provide an estimate of the potential costs of using laboratory-developed IVD tests and our results should therefore be considered as being indicative rather than absolute.

Conclusions
The results of the present study demonstrate that the accuracy of HER2 testing has far-reaching economic, socioeconomic and clinical consequences that need to be considered when a test is requested. Oncologists should be aware that, although HER2-testing methodologies are now numerous, significant differences exist between the various available tests, which may impact on patient safety as well as outcomes. As demonstrated by the NordiQC experience [15], both the approved and laboratory-developed IVD tests can perform well and both can fail; nonetheless, the degree of regulation applied to the approved IVDs reduces the risk of failure with these agents. Adherence to testing guidelines would be expected to reassure the oncologist that accurate results can be obtained and that patients are subsequently treated correctly and not subjected to the risks associated with inappropriate therapy.

We propose that diagnostic tests impacting directly on treatment decisions, ie companion diagnostics, should be subject to in-depth regulatory scrutiny in order to ensure that all patients receive appropriate treatment. It is equally important that treatments are not incorrectly prescribed, as many recently developed agents can be very costly and may have undesired effects if used to treat the wrong patients. It is vital that the accuracy and reliability of companion diagnostic tests be maximised and that the cut-offs are validated, ideally in clinical trials or at least in prespecified analyses of retrospective samples from prospectively conducted clinical trials. Only with this level of scrutiny will patients receive the appropriate treatment and benefit from the treatment advances made in recent years.
conclusions. SN is the scheme manager and RR is the scheme organiser. BS, JR-M and EW are employed by Ventana Medical Systems. JG is employed by Roche Professional Diagnostics. VT and U-PR are employed by F. Hoffmann-La Roche Diagnostics Division.

Acknowledgements
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References
Appendix C: NSH Response to RFI CMS-3326-NC

HQIP Data
Data supporting the claim that NSH/CAP HQIP has associated poor tissue processing to poor routine Hematoxylin & Eosin staining (H&E).
# Appendix C: NSH Response to RFI CMS-3326-NC

## College of American Pathologists/National Society for Histotechnology

### Quality Improvement Program (HQIP)

### Data from HQIP-BX Series

### 2015-B College of American Pathologists (CAP) HQIP Biopsy (Bx) Series

**Effect of Pre-analytic processes (left)**

**Diagnostic Staining (Right)**

### Prostate bx.

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Appendix D: NSH Response to RFI CMS-3326-NC

Citations 7-11
Summary of citations listed on page 3 in the NSH Response to CMS-3326-NC
The Division of Pathology and Laboratory Medicine at The University of Texas MD Anderson Cancer Center has implemented a professional development model designed to further the education, expertise, and experiences of medical laboratory scientists in the core laboratory. The professional development model (PDM) has four competency levels: Discovery, Application, Maturation and Expert. All levels require the medical laboratory scientist to learn new skill sets, complete task and projects, and meet continuing education and certification requirements. Each level encourages personal development, recognizes increased competencies, and sets high standards for all services provided. Upon completion of a level within a given timeframe, the medical laboratory scientist receives a salary adjustment based on the competency level completed.


OBJECTIVE: The study was undertaken to assess educators', practitioners', and managers' perceptions of the future job expectations of clinical laboratory scientists (CLSs) and their opinions on the skills that are expected of CLSs at entry-level and with experience. DESIGN: Survey participants were given a list of 44 competencies related to clinical laboratory science (CLS) practice and were asked whether they would expect a graduate of a respected CLS program to perform each competency in one of three educational categories: the first year of practice, with three to five years of experience but no additional education, or with three to five years of experience plus additional education. The competencies were subclassified into one of four major management functions: laboratory operations, human resource management, financial operations, or communications/consultation. Surveys also included eight Lickert-type questions designed to assess the respondents' opinions on the future job expectations of CLS practitioners. PARTICIPANTS: The sample for the survey included 280 directors of CLS educational programs, 600 managers randomly selected from the Clinical Laboratory Management Association (CLMA) membership, and 600 practitioners randomly selected from the American Society for Clinical Laboratory Science (ASCLS) membership. MAIN OUTCOME MEASURES: The percent of respondents selecting each educational category was tabulated and each competency was assigned to one educational category based on the highest percent of respondents selecting that category. The means of the responses to the Lickert-type questions were calculated for all respondents and for each group of respondents (educators, managers, and practitioners). RESULTS: Response rates of 58% (educators), 28% (practitioners), and 39% (managers) were obtained. Of the 44 competencies in the survey, four were expected at career-entry, 17 were expected of CLS graduates with work experience but no additional education, and 23 were expected of CLS graduates with experience plus additional education. Competencies expected in the first year of practice were primarily scientific and technical. With three to five years of practice and no additional education, the expectations for practitioners were primarily in laboratory operations and communications/consultation areas. The majority of the human resource management and financial operations competencies were expected with three to five years of practice and additional education. All participants agreed that CLS staff-level practitioners need more management and administrative skills and that, in the future, CLS practitioners will spend less time performing laboratory tests and more time solving problems. CLS managers were more positive than CLS educators in response to statements asserting that CLT practitioners and non-certified personnel will have an increased role in the laboratory in the future. CONCLUSION: This
Appendix D: NSH Response to RFI CMS-3326-NC

A study suggests that extensive laboratory operations and communication skills are expected of CLS graduates without any additional education beyond their CLS programs. CLS educators should adequately address those areas in the curriculum. Competence in other non-technical skills may not be expected without the benefit of post-baccalaureate education and in these areas, CLS programs can provide a foundation for future learning.


OBJECTIVE: This study assessed the relationship between the educational preparation and career expectations of CLS students and their subsequent retention in the laboratory profession.

DESIGN: Survey participants were given a list of 32 tasks that may be expected of early career professionals. Participants were asked to rate their educational preparation for and how frequently they performed each task in their current job using a four point Lickert scale.

Additional questions addressed the participants' preparation for their current jobs, career satisfaction, plans for staying in the profession, and factors that influence retention.

PARTICIPANTS: The survey sample consisted of 972 Clinical Laboratory Scientists who passed the National Credentialing Agency for Laboratory Personnel (NCA) CLS examination between June 2002 and June 2004.

MAIN OUTCOME MEASURES: The mean rating for the level of preparation and the frequency of use for each of the 32 competencies was calculated. The mean ratings were used to assess the educational preparation in each competency and identify areas in which the level of preparation did not match the need for that skill in current practice. Using analysis of variance, respondents' answers to questions on their number of years of experience, their plans to stay in the profession, and their job satisfaction were compared based on their perceived level of preparation and the degree to which they felt their current jobs matched their career expectations at graduation.

RESULTS: The response rate was 31%. Most of the respondents felt that they were well prepared for the responsibilities of their current laboratory position. There was a good match between the respondents' ratings of their preparation in each competency and the frequency with which they were required to perform that competency. Phlebotomy and flow cytometry appeared to have more preparation than respondents felt they needed. Troubleshooting, resolving problems, and performing multiple tasks were identified as areas in which more preparation was needed. The mean number of years that respondents planned to stay in the profession was 15.5 years and the factors that were most important in keeping them in the profession included interesting work, good salaries, and advancement opportunities. The respondents who rated the match between their career-entry expectations and their current job the highest were more satisfied and planned to stay in the profession the longest.

CONCLUSION: Early career laboratory professionals felt well prepared for their jobs, though teaching of some tasks could be improved to better prepare graduates for the work environment. Most respondents indicated that they were prepared to stay in the profession for at least ten years; however they indicated that interesting work, good salaries, and opportunities to advance in the profession would be important in their decision to stay. A good match between laboratory employees' career expectations at the time of graduation and their work environment appears to improve their satisfaction with their careers and their desire to stay in the profession.

OBJECTIVE: To survey employee competence assessment practices in departments of pathology and laboratory medicine and provide suggestions for improvement. DESIGN: A 3-part study consisting of a questionnaire about current competence assessment practices, an evaluation of compliance with stated competence assessment practices using personnel records of 30 employees, and a written appraisal of competence of 5 specimen-processing staff members per institution. SETTING: A total of 522 institutions participating in the College of American Pathologists 1996 Q-Probes program. MAIN OUTCOME MEASURES: Institutional competence assessment practices, compliance of each institution with their own practices, and determination of competence of specimen-processing personnel. RESULTS: Of the participating institutions, 89.8% had a written competence plan and 98.1% reported reviewing employee competence at least yearly. General competence was reviewed by direct observations (87.5%), review of test or quality control results (77.4%), review of instrument preventive maintenance (60.0%), written testing (52.2%), and/or other methods (20.8%). In 8.6% of institutions, employees who failed competence assessment were not allowed to continue their usual work. On review of records of 14,029 employees for adherence to the laboratory’s general competence plan, adherence was 89.7% for direct observations, 85.8% for review of quality control and test results, 78.0% for review of instrument records, and 74.0% for written testing. Employee failure rate ranged from 0.9% to 6.4%, depending on the competence evaluated. Adherence to an institution’s plan was 90.4% for new employees, 93.1% for computer skills, 95.8% for laboratory safety, and 92.1% for continuing education. When a written competence assessment was given to 2,853 specimen-processing staff members, 90.0% responded satisfactorily. CONCLUSIONS: Opportunities for improvement in employee competence assessment are numerous, and we provide several specific suggestions.


BACKGROUND: Research in several professional fields has demonstrated that delays (time lapse) in taking certification examinations may result in poorer performance by examinees. Thirteen states and/or territories require licensure for laboratory personnel. A core component of licensure is passing a certification exam. Also, many facilities in states that do not require licensure require certification for employment or preferentially hire certified individuals. OBJECTIVE: To analyze examinee performance on the American Society for Clinical Pathology (ASCP) Board of Certification (BOC) Medical Laboratory Scientist (MLS) and Medical Laboratory Technician (MLT) certification examinations to determine whether delays in taking the examination from the time of program completion are associated with poorer performance. METHODS: We obtained examination data from April 2013 through December 2014 to look for changes in mean (SD) exam scaled scores and overall pass/fail rates. First-time examinees (MLS: n = 6,037; MLT, n = 3,920) were divided into 3-month categories based on the interval of time between date of program completion and taking the certification exam. RESULTS: We observed significant decreases in mean (SD) scaled scores and pass rates after the first quarter in MLS and MLT examinations for applicants who delayed taking their examination until the second, third, and fourth quarter after completing their training programs. CONCLUSIONS: Those who take the ASCP BOC MLS and MLT examinations are encouraged to do so shortly after completion of their educational training programs. Delays in taking an exam are generally not beneficial to the examinee and result in poorer performance on the exam.
Appendix E: NSH Response to RFI CMS-3326-NC:

Histological Prep Complexity Scoring.
Appendix E: NSH Response to RFI CMS-3326-NC

### Histologic Prep Quality
There is a written procedure that describes the process by which pathologists or their designees provide feedback to the histology laboratory on the quality of histologic preparations. This procedure must include the daily recording of the quality of the histologic preparations for each day of tissue processing and slide preparation.

**NOTE:** Histologic preparations refer to H & E sections, histochemical stains, immunohistochemistry preparations, and in situ hybridization preparations.

This requirement applies to laboratories that process and interpret histologic preparations at the same location, as well as laboratories that interpret histologic preparations processed at another laboratory (regardless of that outside laboratory’s accrediting organization).

Records of such feedback and corrective action taken when problems are identified may be incorporated into the laboratory’s quality management program.

(ANP.10042)

#### Histotechnician Competency

<table>
<thead>
<tr>
<th>CLIA Categorization Criteria^2</th>
<th>CLIA Score Assigned</th>
<th>Complexity^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Knowledge</td>
<td>1</td>
<td>13-High</td>
</tr>
<tr>
<td>2-Training and experience</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3-Reagents and Materials</td>
<td>3</td>
<td></td>
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<tr>
<td>preparation</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>4- Characteristics of operational steps</td>
<td>5</td>
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</tr>
<tr>
<td>5-Calibration, quality control, and proficiency testing materials</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>6-Test system Troubleshooting and equipment maintenance</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>7-Interpretation and judgment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Tissue Processing

#### Tissue Processor Solutions

Tissue processor solutions are changed at intervals appropriate for the workload. (ANP.23100)

#### Tissue Processing Programs

Tissue processing programs are validated.

**NOTE:** To validate new processing programs, laboratories should run tissue samples of the same size, thickness and fixation in duplicate. Reagents on the processor(s) should be comparable, e.g. all fresh reagents. Process, embed, cut, and stain slides at the same time and evaluate the quality of the blocks, e.g. firmness, ease of cutting. The slides should be evaluated by the pathologist without knowledge of which processing program was used and graded on quality of section and staining. The new processing program must be of adequate quality before being put into use.

This method may also be used to verify a routine processing program before putting a new processor into clinical service. (ANP.23120)

### Tissue Processing Programs

Specific tissue processing programs are available for different types and sizes of specimens.

**NOTE:** To achieve acceptable results for diagnostic purposes, processing programs may be needed for different sizes and types of specimens. Biopsy specimens may be processed on a shorter schedule than larger specimens; large, dense or fatty specimens and brain specimens will not process adequately on a shorter schedule. A variety of processing programs should be used to achieve good processing results. (ANP.23130)

### Tissue Embedding

1. Recognizes adequacy of processing
2. Maintains accurate identification of the specimen
3. Identifies and orients specimens correctly
4. Identifies the correct mold size for the specimen and use correct orientation when embedding tissue

1. Knowledge
2. Training and experience
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
7. Interpretation and judgment

(ANP.23140)
### Microtomy

1. Determines block orientation and facing in order to obtain a representative section
2. Demonstrates the ability to determine acceptable vs. unacceptable sections
3. Demonstrates the ability to recognize and evaluate instances in which a specific tissue might require a deviation from standard procedure(s) in order to insure that a diagnostic section is produced
4. Slides are of sufficient quality for diagnosis.
   - Criteria to evaluate include adequate tissue fixation, processing, thickness of sections, absence of interfering tissue folds and tears, and good staining technique and cover slipping. The sections must be cut from sufficient depth in the block to include the entire tissue plane. (ANP.11734)¹

5. **Paraffin and Flotation Baths** (ANP.23350)¹
   - Paraffin and flotation baths are clean and well-maintained, and there is a procedure for preventing cross-contamination of glass slides from floaters (fragments of prior paraffin tissue sections) in the flotation bath.
   - **NOTE 1:** Of particular importance are periodic water changes or blotting of the water surface so that sections from one patient block are not inadvertently carried over to another case (so-called "floaters" or "extraneous tissue").
   - **NOTE 2:**
     1. Instruments must be clean and well-maintained (e.g. tissue processors, embedding centers, dispensers and flotation baths)
     2. The temperature of the dispenser must be correct for the type of paraffin used.

6. **Microtome Maintenance** (ANP.23400)¹
   - Microtomes and microtome knives are clean and well-maintained.
   - **NOTES:**
     1. Microtomes must be clean, properly lubricated, and without excessive play in the advance mechanism
     2. Knives must be sharp and free of nicks

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<table>
<thead>
<tr>
<th>Characteristics of operational steps</th>
<th>1-Knowledge</th>
<th>2-Training and experience</th>
<th>3-Reagents and Materials preparation</th>
<th>4-Calibration, quality control, and proficiency testing materials</th>
<th>5-Calibration, troubleshooting and equipment maintenance</th>
<th>6-Test system troubleshooting and equipment maintenance</th>
<th>7-Interpretation and judgment</th>
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<tr>
<td>1. Calibration, quality control, and proficiency testing materials</td>
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<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>5. Test system troubleshooting and equipment maintenance</td>
<td>3</td>
<td>3</td>
<td>3</td>
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</table>
### H&E Stain Quality
1. Selects appropriate stains and chemicals to perform H&E staining procedures
2. Demonstrate the ability to do H&E staining and decide whether stain is acceptable or unacceptable using the microscope.
3. Identifies and corrects problem areas that result in inadequately/improperly stained tissues
4. Slides are of sufficient quality for diagnosis.
   a. Histopathology slides must be of adequate technical quality to be diagnostically useful. For hematoxylin and eosin and other routine stains, the patient slide serves as the internal control to ensure adequate staining technique. (ANP.11734)¹

### Special Stain Quality
1. Demonstrates the ability to determine acceptable vs. unacceptable stains
2. Identifies and corrects problem areas that result in inadequately/improperly stained tissues
3. Slides are of sufficient quality for diagnosis.
4. All histochemical stains are of adequate quality, and daily controls are demonstrated on each day of use for the tissue components or organisms for which they were designed.

NOTE: Positive tissue controls assess the performance of the special stain. Special stains are performed on sections of control tissue known to contain components specific to each special stain. Verification of tissue used as a positive control must be performed and documented before being used with clinical specimens. (ANP.21450)²

<table>
<thead>
<tr>
<th>1-Knowledge</th>
<th>2-Training and experience</th>
<th>3-Reagents and Materials preparation</th>
<th>4-Characteristics of operational steps</th>
<th>5-Calibration, quality control, and proficiency testing materials</th>
<th>6-Test system Troubleshooting and equipment maintenance</th>
<th>7-Interpretation and judgment</th>
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</tr>
</tbody>
</table>

17-High complexity

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¹ANP.11734 (H&E Stain Quality)
²ANP.21450 (Special Stain Quality)
## IHC Staining

### Special Stains/Studies (ANP.21395)

<table>
<thead>
<tr>
<th>IHC Staining</th>
<th>1-Knowledge</th>
<th>2-Training and experience</th>
<th>3-Reagents and Materials preparation</th>
<th>4-Characteristics of operational steps</th>
<th>5-Calibration, quality control, and proficiency testing materials</th>
<th>6-Test system Troubleshooting and equipment maintenance</th>
<th>7-Interpretation and judgment</th>
<th>18-High complexity</th>
</tr>
</thead>
<tbody>
<tr>
<td>For special stains, including histochemical stains, and studies using immunologic and ISH methodology, positive and negative controls are verified and recorded as acceptable prior to or concurrent with the reporting of patient results and records maintained.</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<td>7</td>
<td>18</td>
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<tr>
<td>NOTE: Controls must be verified and recorded as acceptable by a pathologist or designee (provided the designee meets high complexity testing qualifications). Positive tissue controls must contain the component specific to the special stain that is being applied to the specimen. Immunohistochemical tests using polymer-based detection systems (biotin-free) are sufficiently free of background reactivity to obviate the need for a negative reagent control and such controls may be omitted at the discretion of the laboratory director following appropriate validation.</td>
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</table>

### Specimen Modification

If the laboratory performs immunohistochemical staining on specimens other than formalin-fixed, paraffin-embedded tissue, the written procedure describes appropriate modifications for other specimen types. NOTE: Such specimens include frozen sections, air-dried imprints, cytocentrifuge or other liquid-based preparations, decalcified tissue, and tissues fixed in alcohol blends or other fixatives. (ANP.22300)

### Buffer pH

The pH of the buffers used in immunohistochemistry is routinely monitored. NOTE: pH must be tested when a new batch is prepared or received. (CAP ANP.22500)

### QC: Positive Controls

(ANP.22550)

- Appropriate positive controls are used.
  - Written procedure for the selection and use of positive tissue controls for each antibody AND
  - Patient reports or worksheet with control results

### QC: Negative Controls

(ANP.22570)

- Appropriate negative controls are used.
  - NOTE: Negative controls must assess the presence of nonspecific staining in patient tissue as well as the specificity of each antibody with the exception listed below. Results of controls must be documented, either in internal laboratory records, or in the patient report. A statement in the report such as, "All controls show appropriate reactivity" is sufficient.

For laboratories using older biotin-based detection systems, it is important to use a negative reagent control to assess nonspecific or aberrant staining in patient tissue related to the antigen retrieval conditions and/or detection system used. A separate section of patient tissue is processed using the same reagent and epitope retrieval protocol as the patient test slide, except that the primary antibody is omitted, and replaced by any one of the following:
### Antibody Validation

The laboratory has records of validation of new antibodies, including introduction of a new clone, prior to use for patient diagnosis or treatment.

NOTE: The performance characteristics of each assay in the immunohistochemistry laboratory must be appropriately validated before being placed into clinical use. The initial goal is to establish the optimal antibody titration, detection system, and antigen retrieval protocol. Once optimized, a panel of tissues must be tested to determine the assay's sensitivity and specificity. The scope of the validation is at the discretion of the laboratory director and will vary with the antibody. (ANP.22750)¹

### New Reagent Lot Confirmation of Acceptability

The performance of new lots of antibody and detection system reagents is compared with old lots before or concurrently with being placed into service.

NOTE: Parallel staining is required to control for variables such as disparity in the lots of detection reagents or instrument function. New lots of primary antibody and detection system reagents must be compared to the previous lot using at least one known positive control and one known negative (ANP.22760)¹

### IHC Assay Performance

Laboratories confirm assay performance when conditions change that may affect performance.

NOTE: Laboratories should confirm assay performance with at least two known positive and two known negative cases when an existing validated assay has changed in any of the following ways: antibody dilution, antibody vendor (same clone), or the incubation or retrieval times (same method).

Laboratories must confirm assay performance by testing a sufficient number, determined by the laboratory director, of cases to ensure that assays consistently achieve expected results when any of the following have changed: fixative type, antigen retrieval method (e.g. change in pH, different buffer, different heat platform), antigen detection system, tissue processing or testing equipment, environmental conditions of testing (e.g. laboratory relocation), or laboratory water supply. (ANP.22780)¹

### Slide Quality

The immunohistochemical stains produced are of acceptable technical quality.

NOTE: The inspector must examine examples of the immunohistochemical preparations offered by the laboratory. A reasonable sample might include 5-10 diagnostic antibody panels. (ANP.22900)¹

### Pipette Accuracy

Pipettes that are used for quantitative dispensing of material are checked for accuracy and reproducibility at defined intervals (at least annually), and results recorded.

NOTE: Pipette checks must be performed following manufacturer’s instructions, at minimum,
and as defined in laboratory procedure. Such checks are most simply done gravimetrically. This consists of transferring a number of measured samples of water from the pipette to a balance. Each weight is recorded, the weights are converted to volumes, and then arithmetic means (for accuracy), and SD/CV (for imprecision) are calculated. Alternative approaches include spectrophotometry or (less frequently) the use of radioactive isotopes, and commercial kits are available from a number of vendors. Computer software is useful where there are many pipettes, and provides convenient records. This checklist requirement does not apply to Class A volumetric pipettes that meet the American Society for Testing and Materials calibration (accuracy) specifications. (ANP:23085)\(^1\)

### PT for HER2, ER, and PgR (ANP.22973)\(^2\)

The laboratory is enrolled in the appropriate CAP Surveys, or other CAP-accepted proficiency testing (PT) program, for HER2, ER, and PgR testing in breast carcinoma. NOTE: HER2 PT is method specific, and laboratories performing HER2 testing by multiple methods must participate in PT for each method. Details are available on the CAP website http://www.cap.org/. Satisfactory performance requires correct responses on at least 90% of graded challenges in each testing event (mailing).

If the laboratory interprets HER2 test results from immunohistochemical stains prepared at another facility, the laboratory must (1) enroll in an appropriate PT survey, (2) send PT materials to the staining facility for preparation, and (3) interpret the resulting stains using the same procedures that are used for patient specimens. If the laboratory interprets ISH stains for HER2 (ERBB2) prepared at another facility, the laboratory must not participate in PT, but must perform an alternative assessment of the test twice annually.


The FDA categorizes diagnostic tests by their complexity—from the least to the most complex: waived tests, moderate complexity tests, and high complexity tests. Diagnostic tests are categorized as waived based on the premise that they are simple to use, and there is little chance the test will provide wrong information or cause harm if it is done incorrectly. Tests that are cleared by the FDA for home or over-the-counter use are automatically assigned a waived categorization.

CLIA categorization is determined after the FDA has cleared or approved a marketing submission. The FDA determines the test’s complexity by reviewing the package insert test instructions, and using a criteria “scorecard” to categorize a test as moderate or high complexity. Each test is graded for level of complexity by assigning scores of 1, 2, or 3 for each of the seven criteria on the scorecard.

A score of 1 indicates the lowest level of complexity, and the score of 3 indicates the highest level. The 7 scores are added together and the tests with a score of 12 or less are categorized as moderate complexity, and those with a score above 12 are categorized as high complexity. The FDA will notify the sponsor—usually within two weeks of the marketing clearance or approval of their CLIA categorization.
Appendix E: NSH Response to RFI CMS-3326-NC

Categorization Criteria

1 - Knowledge
- Score 1. (A) Minimal scientific and technical knowledge is required to perform the test; and (B) Knowledge required to perform the test may be obtained through on-the-job instruction.
- Score 3. Specialized scientific and technical knowledge is essential to perform preanalytic, analytic or postanalytic phases of the testing.

2 - Training and experience
- Score 1. (A) Minimal training is required for preanalytic, analytic and postanalytic phases of the testing process; and (B) Limited experience is required to perform the test.
- Score 3. (A) Specialized training is essential to perform the preanalytic, analytic or postanalytic testing process; or Substantial experience may be necessary for analytic test performance.

3 - Reagents and materials preparation
- Score 1. (A) Reagents and materials are generally stable and reliable; and (B) Reagents and materials are prepackaged, or premeasured, or require no special handling, precautions or storage conditions.
- Score 3. (A) Reagents and materials may be labile and may require special handling to assure reliability; or (B) Reagents and materials preparation may include manual steps such as gravimetric or volumetric measurements.

4 - Characteristics of operational steps
- Score 1. Operational steps are either automatically executed (such as pipetting, temperature monitoring, or timing of steps), or are easily controlled.
- Score 3. Operational steps in the testing process require close monitoring or control, and may require special specimen preparation, precise temperature control or timing of procedural steps, accurate pipetting, or extensive calculations.

5 - Calibration, quality control, and proficiency testing materials
- Score 1. (A) Calibration materials are stable and readily available; (B) Quality control materials are stable and readily available; and (C) External proficiency testing materials, when available, are stable.
- Score 3. (A) Calibration materials, if available, may be labile; (B) Quality control materials may be labile, or not available; or (C) External proficiency testing materials, if available, may be labile.

6 - Test system troubleshooting and equipment maintenance
- Score 1. (A) Test system troubleshooting is automatic or self-correcting, or clearly described or requires minimal judgment; and (B) Equipment maintenance is provided by the manufacturer, is seldom needed, or can easily be performed.
- Score 3. (A) Troubleshooting is not automatic and requires decision-making and direct intervention to resolve most problems; or (B) Maintenance requires special knowledge, skills, and abilities.

7 - Interpretation and judgment
- Score 1. (A) Minimal interpretation and judgment are required to perform preanalytic, analytic and postanalytic processes; and (B) Resolution of problems requires limited independent interpretation and judgment.
Score 3. (A) Extensive independent interpretation and judgment are required to perform the preanalytic, analytic or postanalytic processes; and (B) Resolution of problems requires extensive interpretation and judgment.

Note: A score of 2 will be assigned to a criteria heading when the characteristics for a particular test are intermediate between the descriptions listed for scores of 1 and 3.
Appendix F: NSH Response to RFI CMS-3326-NC:

States/U.S. Territories Licensing Histotechnicians/Histotechnologists

Florida
Hawaii
Louisiana
Nevada
New York
Tennessee
Puerto Rico
State Licensure of Laboratory Personnel
(Policy Number 05-02)

Policy Statement
The American Society for Clinical Pathology (ASCP) believes that states should license laboratory personnel, and that state licensure legislation should ensure that laboratory personnel possess appropriate academic and clinical training, pass competency-based examinations conducted by an approved national certifying organization, and participate in continuing education programs.

Background and Rationale
I. Introduction
Due to the complexity of laboratory medicine and its importance in quality patient care, it is imperative that medical laboratory personnel possess the qualifications necessary to ensure their professional competence. Licensure and certification programs not only set minimum standards for medical laboratory personnel working in clinical laboratories; they also help ensure quality laboratory testing and proper patient care.

In this document ASCP outlines its view that licensure, when combined with certification, can help improve laboratory test quality and maintain laboratory personnel performance and competency. Review of the literature has not revealed any studies that have directly examined the question of whether licensure of laboratory practitioners improves test quality; however, there are studies that provide support for the idea that education, training and/or experience, and certification of laboratory personnel are linked to higher quality testing and performance. For these reasons, ASCP believes that when licensure includes these essential elements, overall test quality will improve.

ASCP supports personnel standards that incorporate certification, licensure, and practice requirements. These personnel standards must include the following essential elements: an appropriate academic degree, acceptable clinical training or work experience; passage of an examination offered by an approved national certification organization; appropriate continuing competency standards; and recognition of ASCP’s professional terminology for laboratory personnel titles.¹

II. Occupational Regulation
Licensure and certification are two forms of occupational regulation. While licensure is generally well understood, certification is not, in part because this term is sometimes used interchangeably with licensure. Certification by governmental entities is also sometimes confused with certification by nongovernmental (private) organizations. The following section compares the differences between certification and licensure.

A. Certification
Certification is a less restrictive form of occupational regulation than licensure. A government or private entity can provide certification. Certification by a governmental entity is often referred to as “title protection.” In general, governmental certification does not deal with the quality of work performed or the competence of persons performing a certain activity; it does not prevent uncertified personnel from performing the same services as “certified” personnel; it simply restricts the right to use a professional or occupational title.²
Laboratory professionals may be most familiar with certification as it relates to professional organizations or non-governmental agencies, such as the ASCP Board of Certification. In this instance, certification is a voluntary process by which the ASCP Board of Certification grants recognition of competency to persons who have satisfied predetermined qualifications, i.e., education, training and/or experience, and passage of a certifying examination. Health care personnel can be certified without being “licensed,” as is the case with many clinical laboratory personnel.

B. Licensure
The most well known type of occupational regulation is licensure. Licensure refers to the right bestowed by a governmental agency or entity to engage in a legally defined occupational scope of practice. With specified exceptions, this form of occupational regulation prohibits non-licensed individuals from providing certain services. Its intent is to “assure the public that practitioners have met the qualifications and minimum competencies required for practice.” Licensure can address the maintenance of a licensee’s skill through continuing education and/or competency requirements. It can also “provide a universal benchmark for entry-level personnel.”

State governments “license” hundreds of professions. One estimate indicates that more than 800 occupations are licensed by one or more states. Among the healthcare occupations and professions licensed by states are physicians, nurses, midwives, physician assistants, radiologic technicians, chiropractors, physical therapists, and pharmacists. Among the non-health care related occupations regulated by the states are painters, general contractors, school bus drivers, barbers, bartenders, dogcatchers, septic system installers, and insurance agents.

It is clear that laboratory operations, including testing, have a major role in assessing and managing patient health; nevertheless, most states do not license laboratory practitioners. As of November 2009, 11 states and one territory license laboratory personnel. These include: California, Florida, Hawaii, Louisiana, Montana, Nevada, New York, North Dakota, Rhode Island, Tennessee, West Virginia, and Puerto Rico. The state of Georgia does not license laboratory personnel but does specify personnel requirements that are more stringent than those required by the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Certification is utilized by every state that licenses laboratory personnel to assess the initial competency of licensure candidates.

C. Complementary Aspects of Licensure and Certification
A careful examination of certification and licensure suggests that these regulations reinforce and complement one another rather than duplicate or compete with each other. Licensure provides the mechanism to accept and extend the concept of certification over time so that continued personnel competency is assured through periodic self-assessment, competency evaluation, and continuing laboratory education skills. Therefore, licensure can be the process through which laboratory personnel competency is continually maintained.

III. Justification for Licensure of Laboratory Personnel

Are the Clinical Laboratory Improvement Amendments’ Personnel Requirements Sufficient?

The Federal Centers for Medicare and Medicaid Services (CMS) regulates all laboratory testing (except research) performed on patients in the United States through CLIA. CLIA provides a number of important patient protections, such as laboratory personnel standards, proficiency testing (PT), quality assessment and control requirements, and cytology testing standards.

The level of personnel skill and training required by the CLIA regulations depends on the complexity level of the testing performed. Complexity levels include waived, moderate and high complexity. In order to perform laboratory testing of waived, moderate or high complexity tests, laboratory personnel must satisfy minimum standards for the level of testing they perform.
The CLIA personnel qualifications for the three categories of tests are:

- **Waived Testing**: Standards: None.
- **Moderate Complexity Testing**: Standards: Minimum requirement is a high school diploma or equivalent and documented training for the testing performed.\(^{10}\)
- **High Complexity Testing**: Standards: Minimum requirement is an Associate degree, including 24 semester hours in science, and completion of either: (1) an accredited or approved clinical laboratory training program, or (2) three months laboratory training in the specialty(ies) in which the individual performs high complexity testing.\(^{11}\)

The personnel standards required by CLIA address only the minimal requirements, and ASCP believes these are insufficient to fully protect patient and public health. For example, CLIA requires only an Associate degree and minimal laboratory training to perform tests of high complexity. Furthermore, the complexity of new test requirements, especially for genetic and molecular testing, is increasing and renders these standards insufficient. State licensure laws can and should provide higher standards. The adoption of higher standards will ensure that patient and public health are better protected.

Another factor that underscores the need for strong personnel standards is the requirement that laboratories must have the appropriate CLIA accreditation, including PT requirements. PT is an important educational and quality assurance tool used “to assist laboratories to identify and solve problems, evaluate personnel, and improve test results.”\(^{12}\) CLIA does not require continuing education except when remediation is necessary after PT failure.\(^{6}\)

### A. Waived Testing Laboratory Issue

CLIA does not have any personnel requirements for waived testing. Furthermore, CLIA does not require direct oversight of waived testing personnel.\(^{13}\) Individuals who perform waived testing may not be properly trained in specimen collection, preparation techniques, and the laboratory testing process.

A 2001 CMS study of facilities that performed waived testing and provider performed microscopy found widespread problems.\(^{13}\) Registered nurses, licensed practical nurses, practicing physicians, and medical assistants performed most of the testing at these facilities; medical laboratory professionals rarely staff these facilities. The documented problematic findings included: (a) 64 percent failed to have and/or follow current manufacturer’s instructions for proper test performance; (b) 32 percent did not perform quality control as required by the manufacturer or the Centers for Disease Control and Prevention; and (c) 7 percent failed to perform required calibration according to the manufacturer’s recommendations. Moreover, 23 percent of waived testing laboratories surveyed did not have valid or appropriate CLIA certificates; 19 percent had inadequately trained or evaluated personnel; 9 percent did not follow the manufacturer’s storage and handling instructions; and 6 percent used expired reagents/test kits. Subsequent studies by CMS provide further evidence of quality problems at waived testing laboratories.

ASCP believes these findings raise concern about the quality of testing performed in these laboratories and the adequacy of CLIA requirements to safeguard public health. A survey of waived testing laboratories conducted by the Department of Health and Human Services Office of Inspector General also found similar problems, including misunderstanding CLIA requirements, untrained staff, and failure to identify incorrect results.\(^{14}\) State licensure can address these CLIA weaknesses by requiring adequate training and certification of laboratory personnel in all laboratories. Alternatively, CLIA could be revised to require waived testing personnel to meet specific personnel requirements, such as specific training, assessments of competency by a qualified laboratory director, and competency assessment by examination.
B. Patient Safety and the Quality of Laboratory Testing

(1) The Benefit of Higher Quality Testing Standards

The justification for “licensure” is to protect the public from significant harm caused by incompetent or poorly trained members of an “occupational group.” Since laboratory tests form the basis for most medical diagnosis and therapy, the potential exists for serious harm from laboratory testing errors. Documenting quality in health care and the impact of personnel standards is often a difficult task, partly due to problems of measuring quality and isolating the independent effect of variables of interest. Quantifying quality has been an issue for the laboratory industry, which for years has been searching for additional indicators to monitor quality.

It appears that only a few studies have considered the relationship between laboratory test quality and laboratory personnel. These studies,15, 16, 17 which examine PT data, lend support to the notion that test quality is influenced by the same requirements that are the foundation of personnel licensure, namely academic education, clinical training and/or work experience, and a competency assessment examination.

One study of California clinical laboratories investigated PT results in physician’s office laboratories (POLs) during calendar year 1996, the first year after the California legislature reduced the previously stringent laboratory testing standards.15 Significant differences were found to exist among POLs, POLs using licensed medical laboratory scientists (formerly known as medical technologists), and non-POL laboratories. It was concluded that the failure rates for PT tests were significantly lower in POLs that included licensed laboratory professionals as part of the laboratory team.

Another study examining the relationship between the accuracy of laboratory PT results and certification16 found that laboratories that employ only certified medical laboratory scientists produce significantly more accurate results on proficiency tests than laboratories that employ only noncertified scientists. They also found that in laboratories employing both certified and non-certified scientists, a greater proportion of certified medical laboratory scientists positively affects the accuracy of PT results.

A Centers for Disease Control and Prevention study in 1994 (the first year of compulsory participation under CLIA) analyzed PT performance by type of testing facility: hospital and independent laboratories (HI) and all other testing sites (AOT).17 The aggregate rate of satisfactory performance for all regulated analytes, tests, and specialties was 97 percent for the HI group and 91 percent for the AOT group. The unsatisfactory performance by the AOT sites on three commonly utilized medical tests [glucose (15 percent), hemoglobin (9.1 percent) and bacteriology (7.2 percent)] was considered particularly notable. The study comments that the U.S. Health Care and Financing Administration (now the Centers for Medicare and Medicaid Services) indicates the staffs of alternative testing sites are less likely than hospital and independent laboratories to include a laboratory professional with training in personnel standards, quality control and quality assurance programs or be directed by a physician exposed to quality laboratory practice principles during training.

That study concluded that “the laboratory and health care community at large must work together to assure all individuals involved in the performance of clinical laboratory testing have the requisite knowledge and experience to provide optimally accurate and reliable test results.” Because state personnel licensure requirements require academic and clinical training as well certification, ASCP believes licensure should enhance laboratory test quality.
Medical diagnosis and therapy greatly depend on laboratory test results, and test result errors expose patients to a significantly higher risk of inaccurate diagnosis and improper treatment. A CMS study of waived testing laboratories indicates that incidents of failure to follow manufacturers’ instructions may occur in as many as 60,000 laboratories and that this may “potentially harm patients.” Without adequate training of laboratory personnel, the likelihood of inaccurate test results increases. A study of problems in laboratory testing in primary care estimates that more than 16 percent of incorrect test results affect patient care. HCFA suggests that these patient care impacts include delays in receiving appropriate care and the possibility that inappropriate or harmful diagnoses or treatments could result in injury or death.

Several well-publicized instances of problems in clinical laboratories in the past few years illustrate how errors in the testing process adversely affected patient health and well being. Both CMS and laboratory accrediting agencies have also encountered serious problems in recent years at laboratories across the United States.

C. Professional Recognition

State licensure of laboratory personnel is an opportunity to increase professional recognition for the individuals who work in our nation’s laboratories. This professional recognition could increase the recruitment of new individuals into laboratory medicine and promote the retention of current laboratory professionals. Licensure can promote a positive image beyond the walls of the laboratory to educate other health care providers, the public, and legislators about the value of laboratory tests in facilitating medical diagnosis and therapy and about the essential role of the entire laboratory team, e.g., pathologists, clinical scientists and other graduate level personnel, medical laboratory scientists, technologists*, and technicians.

IV. Regulatory Burdens and Lessons Learned

While ASCP believes that licensure of laboratory personnel can improve quality testing, ASCP is simultaneously concerned about the potential for some state laws to create inappropriate or unnecessary burdens on the licensure process. Saddling potential licensees, training programs and clinical laboratories with extraneous requirements that have little or no relation to quality can create artificial personnel shortages and cause the closure of accredited academic and clinical training programs. Such requirements can adversely affect patient care, clinical laboratories and laboratory personnel.

When New York established licensure for laboratory personnel, the state imposed a number of extraordinary burdens that have made licensure difficult or impossible for a number of qualified potential licensees and clinical training programs. These requirements have also hampered clinical laboratories in their efforts to appropriately staff their facilities with skilled personnel. Among these burdens was a requirement that accredited academic and clinical training institutions granting degrees or certificates to potential licensee undergo a rigorous state approval process before the state would recognize the academic degrees or clinical training earned at these programs. Moreover, New York’s approval process was not consistent with accreditation requirements. The result was that potential licensees were caught in limbo in disputes between the state, accrediting agencies, and training programs.

* This term includes categorical technologists as well as chemists, cytogeneticists, cytotechnologists, hemato.logists, histotechnologists, immunohematologists (blood bankers), immunologists, microbiologists, molecular biology technologists, and other baccalaureate-level technologists working in a medical laboratory.

** At least one clinical training program is believed to have closed as a direct result of the New York Department of Education training program requirements.
New York also mandates that training programs must provide both “didactic and clinical training.” Since many, if not, most clinical laboratory training programs are not affiliated with a college or university, training at these “independent” programs, even when accredited, are not considered acceptable for purposes of licensure. Because New York has refused to recognize work experience or on-the-job training, the only route to meeting New York’s clinical training requirement appears to be completion of laboratory training at a state-approved, accredited college or university.

Moreover, when California recognized ASCP’s certification examinations, it refused to recognize certifications earned more than five years before the state recognized ASCP’s examinations. The effect has been to discourage certified personnel from seeking employment opportunities in California.

ASCP is unaware of any evidence suggesting that these mandates have any quality benefit. Such requirements needlessly interfere with the licensure process and should be avoided. To guard against unnecessary or inappropriate burdens on the licensure process, ASCP believes that states should keep licensure requirements to the minimum and where appropriate harmonize their requirements with those of recognized accrediting and certification agencies. Moreover, ASCP believes states should accept academic degrees and training credentials granted by institutions that are accredited by an agency recognized by the U.S. Department of Education or U.S. Department of Health as satisfying state academic and clinical training requirements.

Further, in recognizing certification examinations states should recognize ASCP credentials, regardless of when they were earned.

V. Components of Laboratory Personnel Licensure Laws

In order to ensure that state licensure programs will set appropriate standards for excellence in laboratory medicine, certain key elements must be included in state laws or legislation to license laboratory personnel.

A. Academic Education and Clinical Training

The overall competence of laboratory professionals is strongly influenced by the amount of academic education and training they possess. To recognize the importance of competence to patient outcomes, test quality, and personnel qualifications, ASCP developed and approved a policy statement on personnel standards for laboratory professionals in 2004. That policy states that a medical laboratory scientist/technologist should “possess a baccalaureate degree and successfully complete an accredited or approved training program or specified work experience.” A technician should possess an Associate degree, successfully complete an “accredited or approved medical laboratory training program,” and be able to perform high complexity testing.

B. Certification

Certification examinations offer the most reliable, cost-effective means to ensure that laboratory staff are competent. Licensure programs should require laboratory professionals to pass a competency assessment examination, such as that provided by a recognized national certification organization like the ASCP Board of Certification.

C. Grandfather Provisions

To prevent disruption of the medical laboratory workforce, laboratory personnel licensure bills should include “grandfathering provisions” to allow individuals who have established careers as laboratory personnel to continue working at their current professional level. Typically, state licensure laws for laboratory personnel spell out certain criteria allowing an established laboratory practitioner to be licensed. At a minimum, grandfather provisions would need to conform to the requirements specified by CLIA for high complexity testing. This would generally require
laboratory personnel to possess an Associate degree and appropriate clinical laboratory training, but could involve lesser qualifications depending on CLIA’s requirements and the amount of work experience possessed by the laboratory practitioner. Individuals licensed via grandfathering provisions should be certified, provided they are eligible for a state-approved certification examination.

D. Continuing Education

A continuing education requirement should be included in state licensure laws. Continuing education can help maintain the skill level of licensed laboratory personnel (especially as it relates to bioterrorism and new technologies) and is therefore a useful mechanism to ensure patient health and welfare.

E. Scope of Practice

State licensure laws must define the scope of practice for laboratory professionals. The passage of a state licensure law is an opportunity to reaffirm the scope of practice for laboratory professionals and to ensure adequate personnel standards and protection of patient safety and health.

In recent years, a variety of health care practitioners, such as pharmacists, registered nurses, and midwives, have attempted to expand their scope of practice to include performing and/or interpreting laboratory tests as well as directing or owning clinical laboratories. These health care practitioners generally lack the proper training and experience to ensure quality testing. Such persons may also be performing testing without regard to federal and state laws designed to ensure quality testing. Licensure will help protect the laboratory professionals’ scope of practice by guaranteeing that only qualified individuals do testing in all laboratory areas.

ASCP in its policy statement “Scope of Practice Issues Affecting Pathology and Laboratory Medicine” states that:

Every clinical laboratory, regardless of the complexity of testing it performs, should be under the overall medical supervision of a board-certified pathologist. While the pathologist must ultimately be responsible for each laboratory’s medical, scientific, and technical operations, he or she may delegate the management of the laboratory’s technical and administrative operations to other skilled laboratory practitioners, such as a senior certified medical technologist, cytologist, or histotechnologist. In addition, clinical laboratories should rely only on qualified laboratory personnel, i.e., certified medical and other technologists, cytotechnologists, and medical laboratory technicians, to perform laboratory tests and procedures.

ASCP believes that medical laboratory scientists, technologists and technicians should, under the direction of the laboratory director, be able to perform waived, moderate complexity and high complexity testing. ASCP believes that scientists and technologists should be afforded the following scope of practice:

to perform, interpret and correlate laboratory procedures requiring the broad exercise of independent judgment and responsibility with minimal technical supervision. A technologist may maintain equipment and records, establish and implement protocols, select or develop test methodology, perform quality assurance activities related to test performance.

Medical laboratory technicians and other technicians should be provided the following scope of practice:

to perform laboratory procedures according to established and approved protocols that require the limited exercise of independent judgment and interpretation. The technician performs laboratory procedures across the major areas of the laboratory or concentrates activity in an area such as histology.
F. Licensure Compact: Recognizing Out-of-State Licensure

State licensure laws typically contain provisions requiring the licensing state to recognize licenses granted by other states as meeting state licensure requirements, provided the other state's licensure laws are equal to or more stringent than their own. Unfortunately, it appears that a number of states do not consider other state licenses to be their equal. This blocks a valuable route to licensure, particularly for individuals who have been working in laboratory medicine for years and may not be able to meet updated personnel requirements. ASCP believe that by simplifying licensure laws to rely on accredited academic education and clinical training, as proposed in this policy statement, these barriers to interstate employment can be lessened.

VI. Summary

ASCP believes that individual states should license laboratory personnel. The important work performed by clinical laboratory professionals affects the health, safety and welfare of the public. Licensure is an effective tool to encourage laboratory professionals to possess the skills and expertise needed to perform quality testing. It is the foundation that will guarantee that licensed laboratory professionals possess adequate academic and clinical training, pass competency-based examinations, and participate in continuing education programs.

References:

3 Procedures for Examination and Certification. ASCP Board of Registry. 2005.
8 Section 353 of the Public Health Service Act, Subpart 2, Certification of Laboratories 9 42 Code of Federal Regulations Section 493.5 Categories of tests by complexity.
9 42 Code of Federal Regulations Section 493.1423(b)(4)(ii)

16 Lunz, M.E.; Castleberry, B.M.; James, K.; and Stahl, J. The Impact of the Quality of Laboratory Staff on the Accuracy of Laboratory Results. JAMA. 1987; 258: 361-3.


Appendix G: NSH Response to RFI CMS-3326-NC:

Citations 17-19
Cited articles listed on page 7 in the NSH Response to CMS-3326-NC

Context: In 1995, California adopted a bill that brought laboratory laws in line with the 1988 Clinical Laboratory Improvement Amendments' standards for clinical laboratories and mandated a study comparing results in physicians' office laboratories (POLs) with other settings. OBJECTIVE: To determine whether persons conducting tests in POLs produce accurate and reliable test results comparable to those produced by non-POLs. DESIGN: Survey of clinical laboratories using proficiency testing data. SETTING: All California clinical laboratories participating in the American Association of Bioanalysts proficiency testing program in 1996 (n=1110). MAIN OUTCOME MEASUREs: "Unsatisfactory" (single testing event failure) and "unsuccessful" (repeated testing event failure) on proficiency testing samples. RESULTS: The unsatisfactory failure rate for POLs was nearly 3 times (21.5% vs 8.1%) the rate for the non-POLs and about 1.5 times (21.5% vs 14.0%) for POLs that used laboratory professionals as testing or supervisory personnel (P<.001). The POL unsuccessful rate was more than 4 times (4.4% vs 0.9%) the rate for non-POLs and more than twice (4.4% vs 1.8%) the rate for the POLs using laboratory professionals (P<.001). CONCLUSIONS: Significant differences exist among POLs, POLs using licensed clinical laboratory scientists (medical technologists), and non-POLs. Testing personnel in many POLs might lack the necessary education, training, and oversight common to larger facilities. We must better understand the contributing factors that result in the poorer results of POLs relative to non-POLs. In the meantime, patients should be aware that preliminary findings suggest that differences in quality of laboratory tests based on testing site may exist. Laboratory directors at all testing sites must ensure that they understand laboratory practice sufficiently to minimize errors and maximize accuracy and reliability. Directors must understand their obligation when they elect to oversee those assigned testing responsibility. Legislators may wish to reconsider the wisdom of further easing restrictions on those to whom we entrust our laboratory specimens.


This study tests the premise that laboratories employing medical technologists certified by the Board of Registry of the American Society of Clinical Pathologists (MT[ASCP]) produce more accurate laboratory test results, as measured by the College of American Pathologists proficiency tests. Licensed laboratories in Illinois provided the sample. An accuracy score on the College of American Pathologists proficiency tests was calculated for each laboratory. The accuracy score of a subgroup of laboratories employing all (100%) certified medical technologists was compared with the accuracy score of a subgroup of laboratories employing only noncertified medical technologists. Those laboratories employing only certified medical technologists had a mean accuracy score of 95% (SD = 4%), while laboratories employing only noncertified medical technologists had a mean accuracy score of 75% (SD = 30%). The Mann-Whitney U test was used to identify differences between the two groups of laboratories. A difference in the accuracy scores between the two groups of laboratories was statistically discernible. Since most laboratories
employ some certified medical technologists, a second analysis considered the relationship of the proportion of certified medical technologists employed in the laboratory and accuracy on College of American Pathologists proficiency tests. A significant positive Spearman rs correlation confirmed a relationship between employing a higher proportion of certified medical technologists and accuracy of test results.


Congress enacted the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to promote uniform quality and standards among all testing sites in the United States. The performance indicators specified in the legislation are proficiency testing (PT) performance and periodic inspections. **OBJECTIVE:** To evaluate variation in PT performance by type of testing facility during the first year of compulsory participation under CLIA. **DESIGN:** All 1994 PT score data electronically reported to the Health Care Financing Administration as a component of compliance with the CLIA regulations were obtained. Over 1.2 million PT event scores from 17058 unique testing sites were sorted into 2 groups based on the type of testing facility: hospitals and independent laboratories (HI) and all other testing sites (AOT). **MAIN OUTCOME MEASURES:** Satisfactory and unsatisfactory performance rates for HI and AOT for each analyte and/or test, according to the criteria specified by the CLIA regulations. **RESULTS:** The aggregate rates of satisfactory event performance for all regulated analytes, tests, and specialties were 97% and 91% for the HI and AOT groups, respectively. The aggregate odds ratio for unsatisfactory PT event performance for the AOT group compared with the HI group was 2.89, with a range of 2.19 to 7.51 for the individual analytes. **CONCLUSION:** There was a consistent difference in PT performance during the first full year of compulsory PT under the CLIA regulations based on the type of testing facility performing the analysis. Traditional testing sites achieved higher rates of satisfactory performance than newly regulated, alternative testing sites.