

Clinical Laboratory Improvement Advisory Committee

Summary Report

**September 1-2, 2010
Atlanta, Georgia**

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

**Clinical Laboratory Improvement Advisory Committee
September 1-2, 2010 Summary Report
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Record of Attendance

Committee Members Present

Ms. Elissa Passiment, Chair
Dr. Ellen Jo Baron
Dr. Christine Bean
Ms. Susan Cohen
Dr. Judy Daly
Dr. Nancy Elder
Dr. John Fontanesi
Ms. Julie Gayken
Dr. Geraldine Hall
Dr. Norman Harbaugh, Jr.
Dr. Paul Kimsey
Dr. James Nichols
Dr. Stephen Raab
Dr. Linda Sandhaus
Dr. Paula Santrach
Dr. Gail Vance
Dr. Emily Winn-Deen
Dr. Rosemary Zuna
Ms. Luann Ochs, AdvaMed (Liaison Representative)

Committee Members Absent

Dr. Gary Overturf

Executive Secretary

Ms. Nancy Anderson

Designated Federal Official

Dr. Tom Hearn, CDC

Ex Officio Members

Dr. Alberto Gutierrez, FDA
Dr. Roberta Carey, CDC
Ms. Judith Yost, CMS

Record of Attendance - cont'd.

Centers for Disease Control and Prevention (CDC)

Mr. Todd Alspach	Ms. Anne Pollock
Dr. Rex Astles	Ms. Cheri Rice
Ms. Diane Bosse	Dr. John Ridderhof
Dr. Salvatore Butera	Ms. Colleen Shaw
Dr. Carlin Collins	Dr. Shahram Shahangian
Dr. Bin Chen	Mr. Darshan Singh
Ms. MariBeth Gagnon	Ms. Theresia Snelling
	Dr. Susan Snyder
Dr. Devery Howerton	Ms. Heather Stang
Mr. Jeffery Jarrett	Dr. Shambavi Subbarao
Dr. Lisa Kalman	Ms. Marissa Scalia Sucusky
Ms. Debra Kuehl	Dr. Julie Taylor
Dr. Ira Lubin	Mr. Howard Thompson
Ms. Leslie McDonald	Ms. Pam Thompson
Ms. Andrea Murphy	Ms. Irene Williams
Dr. James Peterson	Ms. Yasmine Zavahir

Department of Health and Human Services (Agencies other than CDC)

Ms. Carol Benson (FDA)	Dr. Marina Kondratovich (FDA)
Mr. James Cometa (CMS)	Mrs. Melissa Singer (CMS)
Dr. Elliot Cowan (FDA)	Ms. Debra L. Sydnor (CMS)
Ms. Valeria Coppola (CMS)	Ms. Kathleen Todd (CMS)
Ms. Karen Dyer (CMS)	Mrs. Harriet Walsh (CMS)
Mrs. Penny Keller (CMS)	Ms. Cheryl Wiseman (CMS)

In accordance with the provisions of Public Law 92-463, the meeting was open to the public. Approximately 30 public citizens attended one or both days of the meeting.

Clinical Laboratory Improvement Advisory Committee

The Secretary of Health and Human Services is authorized under Section 353 of the Public Health Service Act, as amended, to establish standards to assure consistent, accurate, and reliable test results by all clinical laboratories in the United States. The Secretary is authorized under Section 222 to establish advisory Committees.

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health regarding the need for, and the nature of, revisions to the standards under which clinical laboratories are regulated; the impact on medical and laboratory practice of proposed revisions to the standards; and the modification of the standards to accommodate technological advances.

The Committee consists of 20 members, including the Chair. Members are selected by the Secretary from authorities knowledgeable in the fields of microbiology, immunology, chemistry, hematology, pathology, and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director, Centers for Disease Control and Prevention; the Commissioner, Food and Drug Administration; the Administrator, Centers for Medicare & Medicaid Services; and such additional officers of the U.S. Government that the Secretary deems are necessary for the Committee to effectively carry out its functions. CLIAC also includes a non-voting liaison representative who is a member of AdvaMed and such other non-voting liaison representatives that the Secretary deems are necessary for the Committee to effectively carry out its functions.

Due to the diversity of its membership, CLIAC is at times divided in the guidance and advice it offers to the Secretary. Even when all CLIAC members agree on a specific recommendation, the Secretary may not follow their advice due to other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the regulations, the reader should not infer that all of the Committee's recommendations will be automatically accepted and acted upon by the Secretary.

CALL TO ORDER – INTRODUCTIONS/FINANCIAL DISCLOSURES

Dr. Thomas Hearn, Designated Federal Official, Clinical Laboratory Improvement Advisory Committee (CLIAC), and Deputy Director, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), CDC, welcomed the Committee and the members of the public, acknowledging the importance of public participation in the advisory process. He explained the meeting would primarily address issues of laboratory proficiency testing. After noting it was this topic that brought him to CDC many years ago, he described it as an important part of laboratory testing grounded in science that is

intended to separate the laboratories that do a good job from those that need some serious attention.

Dr. Hearn further stated the meeting would initially focus on cytology proficiency testing and workload recording; there would be a segment on the electronic exchange of laboratory information; and the remainder of the time would be presentations and a discussion of a report from the CLIAC Proficiency Testing Workgroup.

Dr. Hearn introduced five CLIAC members who were to receive plaques and letters of appreciation for the time and effort required to serve on the Committee. These included Dr. Nancy Elder, Dr. Geraldine Hall, and Dr. James Nichols, who were photographed with Dr. Hearn receiving their plaques, and Dr. Gary Overturf and Dr. Gerald Schwarz who were absent from this meeting.

Ms. Elissa Passiment, Chair, CLIAC, welcomed the Committee and called the meeting to order. All members then made self-introductions and financial disclosure statements relevant to the meeting topics.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Food and Drug Administration (FDA) Update

Alberto Gutierrez, Ph.D.

[Addendum A](#)

Director, Office of In-Vitro Diagnostic Device Evaluation and Safety (OIVD)

Center for Devices and Radiological Health

Food and Drug Administration

Dr. Gutierrez provided an update on the organizational changes and current initiatives at the FDA Agency and Center levels. Among the Center's initiatives were a program review of the 510(k) review process in an effort to strengthen this process, notification of direct-to-consumer genetic testing manufacturers to inform them of the need to comply with FDA requirements for marketing *in vitro* diagnostic (IVD) devices, and a plan to address the need for oversight of laboratory developed tests. With respect to new guidance, OIVD recently published frequently asked questions for IVD device studies and recommendations for premarket notifications for lamotrigine and zonisamide assays. Among FDA's notable 510(k) clearances, Abbott obtained a 510(k) clearance on newly developed glucose test strips to replace those with reported drug interference problems. Two tests for the detection of H1N1 influenza were cleared, allowing for H1N1 testing post expiration of the emergency use authorization on June 23, 2010. The Oncology Drug Advisory Committee (ODAC) voted in favor of an FDA review prior to approval of the omacetazine drug test making it the first test of its kind requiring FDA review. Of several recalls listed, the first voluntarily FDA-approved laboratory developed test was recently subject to a recall due to changes in raw materials. Several warning letters were sent by OIVD to manufacturers with quality concerns as well as letters sent to manufacturers of hemoglobin A1c tests inviting them to work with OIVD in obtaining

510(k) clearance. Among public meetings, a workshop on blood glucose testing was held in March to discuss whether the current accuracy standards for blood glucose meters are acceptable. On August 26th CDC, FDA, and CMS collaborated to issue a medical alert on the use of fingerstick devices after several incidents in which devices were re-used and resulted in transmittal of blood borne pathogens. Dr. Gutierrez concluded his presentation with a discussion on the medical device user fee program that expires in September 2012 with a public meeting scheduled for September 14, 2010, to obtain input from stakeholders as FDA considers the next user fee program.

Committee Discussion

- A Committee member asked what ODAC was. Dr. Gutierrez explained it is the Oncology Drug Advisory Committee which meets regularly to advise the FDA on the approval of oncology drugs.
- A member wanted to know who was required to report device failures to the FDA and what enforcement power the FDA had. Dr. Gutierrez responded that industry notifies the FDA when problems occur and the FDA is available to assist the manufacturer if they request assistance. The FDA verifies that the manufacturer has acceptable systems for the detection of errors, looks for the root cause of problems, and monitors and responds to complaints.
- A member asked what percentage of laboratory tests are not done properly, if the patient can request a test to be repeated, and if the patient can file a complaint. Ms. Yost responded that the patient has a right to ask for a test to be repeated and confirmed CMS does receive and respond to patient complaints. Another member noted that laboratories accredited by the College of American Pathologists (CAP) are required to post the CAP complaint number. Ms. Yost added that CMS has a list of laboratories with imposed sanctions (Annual Laboratory Registry) available on the CMS website as well as a list of all CLIA-certified laboratories. The member responded that most patients are not aware of this and will likely not look at this list.

PRESENTATIONS AND COMMITTEE DISCUSSIONS

CYTOLOGY PROFICIENCY TESTING

National Cytology Proficiency Testing 5-Year Review

Debra Sydnor, CT (ASCP) IAC
Division of Laboratory Services
Survey & Certification Group; CMS/CMSO
Centers for Medicare & Medicaid Services

[Addendum B](#)

Ms. Sydnor presented data, for 2005 to 2009, from the three approved programs in the national cytology proficiency testing (PT) program. She began her presentation with a brief description of the current cytology PT regulations which mandate that each individual involved in screening and interpreting cytologic preparations must participate in annual cytology PT and pass with a score of 90%. The initial test, consisting of 10 glass slides, must be performed within a two hour period; individuals are given four

opportunities to pass. The analysis of the results of the initial tests from 2005 to 2009 showed an improvement in overall performance. In 2009, the pathologists who practice without a cytotechnologist to prescreen the slides had the highest PT failure rate at 12% while the cytotechnologists and the pathologists who practice with a cytotechnologist prescreening the slides both had 3% failure rates. The failure rate of pathologists who practice without a cytotechnologist to prescreen the slides generally improved from the 2005 high of 33% through 2009. Ms. Sydnor noted the number of individuals participating in cytology PT decreased by approximately 485 from 2005 to 2009. This decrease, Ms. Sydnor stated, was likely attributed to the closing of schools, retirement of the workforce, increased use of the human papillomavirus vaccine, and expansion of molecular testing. She also noted a trend where the pathologists practicing without a cytotechnologist to prescreen the slides had decreased while the number of pathologists practicing with a cytotechnologist prescreening the slides showed a slight increase, suggesting that more pathologists were choosing not to screen their own slides. Ms. Sydnor ended her presentation stating that CMS views cytology PT as a successful program that is an asset to women's health and helps to ensure Pap tests are being read by individuals who are properly trained and qualified.

Committee Discussion

A Committee member wanted to know if CMS compared the PT performance results for individuals who screen liquid-based versus glass-slide and automated versus manual Pap slides. CMS responded they had not analyzed the data using those criteria.

National Cytology Proficiency Testing

Cheryl Wiseman, M.P.H., CT (ASCP)
Division of Laboratory Services
Survey and Certification Group
Centers for Medicare & Medicaid Services

Ms. Wiseman described the specialized reviews in cytology that CMS has conducted for the past 22 years under a contract with the American Society for Cytotechnology. In addition to a full CLIA survey, the specialized cytology review includes cytotechnologists who review previously examined slides. If significant diagnostic discrepancies are identified by the cytotechnologists during this review, the survey team leader will call a pathologist to adjudicate. Currently 68 consulting cytotechnologists, who qualify as general supervisors in cytology, perform the surveys with eight pathologists available on call. Since beginning the specialized reviews in 1988, 830 surveys have been performed in 775 laboratories selected either randomly, as a result of a complaint, by nomination from their state or regional office, or by the CMS Central Office. The results from the surveys are sent to the regional offices for any enforcement actions. In addition to diagnostic discrepancies, the surveyors have identified off-label use of two FDA-approved semi-automated screening devices, the Hologic ThinPrep Imaging System and the Becton Dickinson Focal Point Guided Screening System. These devices screen the slides and identify areas that may contain abnormal cells. A cytotechnologist then reviews the areas identified by the devices and determines if a

manual review is needed. Both devices were found to have problems with identifying unsatisfactory slides and certain types of abnormal cells and laboratories were not calculating workload properly when using these screening devices. Ms. Wiseman noted that CMS has been working with the FDA since August 2009 to resolve the problems with the semi-automated screening devices.

Status of Cytology Proficiency Testing Proposed Regulations

Judith Yost, M.A., MT (ASCP)
Director, Division of Laboratory Services
Center for Medicaid and State Operations
Centers for Medicare & Medicaid Services

[Addenda C, D, E, F](#)

Ms. Yost provided the background of the CLIA law and the cytology PT proposed rule published in January 2009. CLIA law mandates that the proficiency of each individual be periodically confirmed and evaluated. This differs from other specialty areas where PT is required of the laboratory rather than the individual. The regulations for cytology PT were implemented in 2005 when the first program was approved by CMS. Since then, concerns and opposition to PT have been expressed within the cytology community resulting in proposed legislation to replace PT with required continuing education (CE). In an effort to respond to the concerns, in 2006 CMS and CDC convened a CLIAC cytology PT workgroup to consider potential modifications that might be made to the cytology PT regulations. After getting input from that workgroup, CLIAC made 16 recommendations to HHS which formed the basis for the 2009 proposed rule published by CMS and CDC. In response to the proposed rule, approximately 6,500 comments were received from about 690 commenters including cytology and laboratory professional organizations, individuals, and advocacy groups. Analysis of the comments showed that 77% of the 690 comments requested the regulation be withdrawn and PT replaced by CE, similar to the format proposed by Congress. CMS could not act on the request to replace PT with required CE because it was not part of the proposed rule and because CE is not within the scope of CMS's authority under the CLIA law. With respect to other public comments received, CMS found there was no discernible consensus in support of many of the proposed changes to cytology PT. However, there was some agreement with seven of the proposed changes and CMS has determined that they can address these issues without changing the regulation by adding information or making changes to the Interpretive Guidelines. In conclusion, Ms. Yost stated CMS recommended withdrawing the proposed rule, keeping the current standards in place, updating the Interpretive Guidelines, and continuing to monitor the performance of cytology PT. The CMS rationale for this recommendation is that cytology PT is identifying individuals who cannot identify abnormal cells and it verifies that most individuals who perform cytology testing do high quality work. She also stated that the combination of PT, specialized surveys, and the cytology quality standards found in CLIA allow CMS to identify and remedy problems as they occur. She asked the Committee to consider CMS's recommendation to withdraw the proposed rule.

Committee Discussion

- A Committee member, while agreeing that improvement over the last 5 years in cytology PT is evident from Ms. Sydnor's presentation, asked the Committee if a 3% failure rate was acceptable. It was pointed out by another member that a 3% failure rate may be a statistical aspect of the test and does not necessarily mean poor performance. The member added that the failure rates seemed to have reached a plateau three years after the initial impact of testing. Ms. Yost responded that initially high failure rates may have resulted from anxiety over a new test. However, pathologists that do not use a cytotechnologist to prescreen slides continue to have a higher failure rate and therefore CMS advocates for continuous monitoring through PT. She added that CMS is identifying trends by looking at the sequential performance of individuals and, in some cases, sending in surveyors to determine whether those individuals with repeat failures are still screening slides and if other problems can be identified. When asked about how many years of cytology PT performance data CMS would like to compile before the Committee reviews this topic again, Ms. Yost replied that a few more years of data should show whether the cytotechnologist and pathologist-with-cytotechnologist groups have reached a plateau, but she cannot predict this for sure.
- A Committee member asked why many of the comments indicated cytology PT should be discontinued while other laboratory PT continues to be required. A member replied that cytology PT is subjective and difficult to standardize with two hours being a limited time to verify performance. Another member pointed out that cytology tests differ from other laboratory tests and suggested an expert committee be engaged to evaluate the future of cytology PT and look for ways to improve it. Ms. Yost agreed cytology PT needs to be maintained but a change in its frequency could possibly be considered. Several members supported the idea of having those individuals with repeat failures perform annual PT while individuals who continue to pass perform less frequent PT. Ms. Yost responded that any proposed changes would need to be supported statistically.
- A member asked what CMS was proposing for the frequency of testing. Ms. Yost replied that the current frequency of testing is annual, as stated in 1992 regulations. Ms. Yost further commented that one of the proposed changes had been to decrease the frequency of testing to once every two years and increase the number of required challenges to 20. Ms. Yost noted that CMS received several comments that referenced current literature stating that a 10 slide test may not be statistically valid and that 100 slides would be required for the test to be considered a statistically valid test. However, the comments were clear that individuals did not want to give up four hours to take the test and would not support the time required to take a test composed of 100 slides.
- A member asked what the estimated annual cost of cytology PT and the cost of identifying one poor performer were. Ms. Yost responded that CMS does not have this information. The PT programs are private organizations and are the only ones that would have this information. She elaborated that cost is considered and included in the impact analysis section of a proposed rule. Ms. Yost added that both cost to the laboratories as well as cost to patients must be considered.
- Ms. Yost asked the Committee if the proposed rule should be withdrawn. Several members said that they were not familiar with the proposed rule and its history and

could not make any determinations at this time. Ms. Yost reminded the Committee that this information was presented at a previous CLIAC meeting. Dr. Hearn and Ms. Anderson added that the previous CLIAC summary and recommendations can be viewed on the CDC CLIA website under the June 2006 CLIAC meeting. Other members noted that the number of comments submitted in opposition to the proposed rule warranted further analysis of the data before a recommendation can be made by the Committee. One member asked what the time frame was for review of the proposed rule and resulting comments by the Committee. Ms. Yost said there is a three year review period adding that the proposed rule was published in 2009.

- A member commented that CMS should analyze the data on failure rates, causes for failure, trending, etc. and present this at the next meeting. If necessary, a workgroup should be formed to analyze the data. Ms. Yost agreed that CMS can provide a requirement comparison in chart form that it is simple and easy to understand.

CLIAC recommendation

- **CMS should analyze the cytology PT data directly in light of concerns expressed by the Committee on failure rates, reasons for failure, and trends and should present to CLIAC at the next meeting along with an analysis of the cytology PT proposed rule and how it addresses these concerns.**

FDA Cytology Update

Marina Kondratovich, Ph.D.

[Addendum G](#)

Associate Director for Clinical Studies

Director, Office of In-Vitro Diagnostic Device Evaluation and Safety

Center for Devices and Radiological Health

Food and Drug Administration

Dr. Kondratovich presented the results of the FDA investigation into problems reported by CMS regarding two FDA-approved semi-automated screening devices for Pap tests, Hologic's ThinPrep Imaging System (TIS) for ThinPrep Pap slides and Becton Dickinson Focal Point Guided Screening System (BD) for SurePath Pap slides. During the approval process for both instruments, clinical studies established the maximum workload limits as 200 slides for TIS and 170 for BD. It was brought to FDA's attention that the workload for these two devices is difficult to interpret resulting in variability and lack of standardization in slide counting methods. Dr. Kondratovich provided an example that demonstrated the upper limit of 200 slides for the TIS was only correct if an average of 22% of the slides required full manual review (FMR) and stated a similar evaluation could be done for BD. The percentage of slides that require FMR on either instrument depends on the prevalence of abnormal slides and unsatisfactory slides, the policy of the laboratory regarding review of high risk slides and the skills of the cytotechnologist. Since the percentage of slides requiring FMR is not the same for every laboratory, it is difficult to set an upper limit that would be consistent across laboratories. Based on this information, FDA and CMS determined that the following method should be used for calculation of workload when using the semi-automated screening devices: slides that require FMR count as 1 slide, slides with a field of view (FOV) only review count as 0.5

slide, and slides with both FMR and FOV count as 1.5 slides. To count workload the formula: $1.5(\# \text{ slides with both FMR and FOV}) + .5(3 \text{ of slides FOV}) + 1(\text{FMR}) \leq 100$ should be used. Dr. Kondratovich concluded her presentation saying that FDA will work with Hologic and BD on labeling changes using the recommended slide counting approach.

Committee Discussion

A Committee member recognized the importance of accurately estimating workload limits since these are included in regulations. However, the member further commented that it is also important to consider the processes used along with the technology used when determining workload because process-related change can improve the quality of testing.

Electronic Health Records and CLIA

Karen Dyer MT (ASCP), DLM
Division of Laboratory Services
Survey and Certification Group
Centers for Medicare & Medicaid Services

[Addendum H](#)

Ms. Dyer provided a definition for an electronic health record (EHR) and stated that it was the Secretary's goal for everyone to have an EHR by 2014. To accomplish this Title IV of the Recovery and Reinvestment Act of 2009 (ARRA) established the Health Information Technology for Economic and Clinical Health Act (HITECH). HITECH created a Federal advisory committee known as the Health Information Technology (HIT) Policy Committee. The HIT Policy Committee has broad representation from major health care constituencies and provides recommendations to the Office of the National Coordinator for Health Information Technology (ONC) on issues relating to the implementation of a nationwide health information infrastructure. Among other efforts, the HIT Policy Committee has sought to identify barriers to the adoption and use of health information technology. According to the HIT Policy Committee, CLIA regulations are perceived by some stakeholders as imposing barriers to the exchange of health information. CMS has worked with the ONC, HIT Policy Committee, Office of General Council, and Office of E-Health Standards and Services to address the CLIA issues thought to hinder the electronic exchange of laboratory information. CMS has updated the Interpretive Guidelines and posted a list of frequently asked questions to address the issues surrounding the laboratory's responsibility in transmittal of test reports. Ms. Dyer explained that CLIA does not regulate EHR systems or vendors and EHR companies are not required to develop products that are CLIA compliant, making the laboratory responsible for determining if their EHR product meets regulatory requirements. Ms. Dyer concluded her presentation indicating that health care reform goals intend to allow patients to become more actively involved in their own health care decisions and to control their personal health information.

Committee Discussion

- A Committee member wished to know how laboratories could be expected to verify that each EHR system meets CLIA requirements when the laboratory is often not the primary selector of the EHR system in use by a hospital. The member opined that EHRs should be regulated under CLIA and another member asked who will certify EHR systems and set the standards for laboratory reporting and interoperability via the EHRs. Ms. Dyer responded that the certification process for EHRs is just beginning and CLIA may become part of this process over time.
- Other members asked whether there was a laboratory representative working with the ONC to assure that complexities concerning laboratory issues and EHRs were understood and taken into consideration. The Chair commented that these issues were discussed during the February CLIAC meeting and explained that while the Committee appreciated CMS efforts, they felt it was important to have a liaison from the laboratory community involved in discussions. Dr. Hearn commented CDC is also involved with ONC on public health initiatives. A member stated that CLIAC needs to be proactively involved with implementation of EHRs and several members voiced concerns that EHR systems were already being implemented without CLIAC's involvement. The Chair responded that a workgroup was proposed for this purpose during the February 2010 meeting.
- A member commented that future control of EHRs may lie in regional hubs or within large entities or organizations instead of with the patient or doctor.
- Ms. Yost acknowledged the support for, and growth of, regional hubs for health information. However, she emphasized CLIA requires a laboratory to assure that test results are transmitted to the individual who ordered the test, the individual who is responsible for a patient's care, or the referral laboratory, if applicable. The results must be delivered accurately, reliably, confidentially, and in a timely manner, and must contain certain elements. She noted that CLIA is only one small piece of the EHR adoption process.
- A member identified a need for a consumer's guide to laboratory tests and presented an example to the Committee for their consideration.

PROFICIENCY TESTING WORKGROUP REPORT

CLIA PT Background

Judith Yost, M.A., MT (ASCP)
 Director, Division of Laboratory Services
 Center for Medicaid and State Operations
 Centers for Medicare & Medicaid Services

Ms. Yost preceded the introduction of the PT Workgroup report by highlighting the PT requirements in Section 353 of Public Law 100-578 subsection (f)(3) and PT referral in subsection (i). She explained that Committee recommendations to update the CLIA PT requirements cannot be more stringent than the law. Reminding the Committee that currently PT is required only for a set number of tests listed in the regulation, Ms. Yost suggested one focus of the discussion be towards the establishment of a scientifically sound process to identify tests for inclusion in the regulations. She also advised CLIAC

to consider areas of the PT regulations that might be outdated or that could be improved. She concluded by urging the Committee to consider, when forming these recommendations, the cost of PT materials, the work burden incurred to perform PT, that test frequency cannot be an exclusive way to select analytes because of the high clinical relevance of certain esoteric tests, and that the PT process is for non-waived testing, about half of which is performed by physician offices.

PT Workgroup Background

Nancy Anderson, MMSc
Chief, Laboratory Practice Standards Branch
Division of Laboratory Science and Standards
Laboratory Science, Policy and Practice Program Office
Office of Surveillance, Epidemiology, and Laboratory Services
Centers for Disease Control and Prevention

[Addenda I, S, T, U, V, W, X](#)

Ms. Anderson began her presentation by providing the background and constituency of the PT Workgroup, and acknowledging the Workgroup Chair, Dr. James Nichols and Microbiology Co-Chair, Dr. Gerri Hall. She restated the Workgroup's charge from CLIAC, "Provide input to CLIAC for their consideration in making recommendations to HHS regarding the need for revisions to the CLIA requirements for PT as specified in subparts H and I of the regulations" and listed the Workgroup's objectives:

- Updating the list of CLIA-regulated analytes
- Revising the criteria for acceptable performance (grading criteria), including target values and acceptable limits for current and proposed analytes
- Changes to specialties or subspecialties that do not have regulated analytes, including microbiology
- Clarification of the requirements that address PT referral
- Other changes needed to update and improve required PT

Ms. Anderson then reviewed the statutory and regulatory PT requirements for non-waived testing and PT program approval. She discussed the regulated analytes in each of the specialties and subspecialties and noted this information is reflected in the CLIA PT brochure (Addendum S). In microbiology, where there are no regulated analytes, PT is required based on "types of services that are offered by laboratories." She provided considerations for revising the list of regulated analytes and summarized past CLIAC discussions regarding inclusion criteria including:

- Impact on patient care/clinical significance of test
- Testing problems with specific analytes
- Cost/benefit analyses for laboratories

Ms. Anderson concluded by pointing out the data and information provided for Committee consideration when determining recommended criteria by which analytes are added to the list of regulated analytes. Addendum X contains the complete list of the final CLIAC recommendations for revisions to the CLIA requirements for PT.

Workgroup Report – Analyte Inclusion/Prioritization

James Nichols, Ph.D., DABCC, FACB
Professor of Pathology
Tufts University School of Medicine
Medical Director, Clinical Chemistry
Baystate Health

[Addendum J](#)

Dr. Nichols reported on the 2010 Proficiency Testing Workgroup meeting. He discussed the PT issues raised by the Workgroup members, then presented the first series of questions (slides 1-29) addressed by the Workgroup along with their input on the issues of:

- Factors for adding regulated analytes
- Assessing factors or criteria for analyte inclusion
- Number of analytes to add
- Required PT for other specialties
- Data for analyte inclusion
- Analytes for consideration
- Impact of additional required PT
- Process for adding PT analytes
- Deletion of required PT analytes
- PT of the total testing process
- Method based PT

Committee Discussion

The Chair requested feedback from the Committee on the first portion of the Workgroup report including how the criteria might be prioritized. The following represents a per-issue summary of options for regulatory revision with the respective questions posed to the Workgroup, the Committee's deliberations, and final CLIAC recommendations.

Factors for Adding Regulated Analytes

What factors should be considered for adding regulated analytes to subpart I of the CLIA PT regulations?

Committee Discussion

- Several members concurred PT should be required for all analytes and reminded the Committee that many laboratories already perform PT for analytes not on the CLIA-regulated list, either as a voluntary quality assurance measure or because they are required to do so as accredited laboratories. However, the Chair raised the concern of cost to laboratories if PT was required for every analyte tested for by laboratories, especially considering microarrays or new technologies that have the capacity to test for many analytes. The Committee considered clinical relevance and whether material is available for PT to be two primary factors for inclusion as a regulated analyte. For the proposed criteria of testing volume, a member cautioned that in some analyses, such as genetic testing, volume may be low but testing outcomes have enormous consequences.
- The Chair asked whether the list of regulated analytes in the CLIA regulations should be modified to include all moderate or high complexity tests. Many members

responded no, the list of analytes provides clarity. Another member cautioned that implementation of a requirement for PT for all moderate and high complexity testing would be overwhelming, adding that total quality management and different approaches to ensure laboratory quality must be considered. Dr. Hearn also reemphasized PT is just one part of the quality management system.

- One member expressed concern that if the analyte list is included in the regulations, it would be immutable until revised. Several members recommended the regulations be revised to refer to a flexible list of analytes. Another member suggested having the current, correct list outside of the regulations to facilitate continuous updating if this is legally possible. Ms Yost emphasized the fact that if an analyte is removed from the regulations, enforceability may not be possible and that CMS would need to investigate this further. She and others agreed it is important first to look at criteria for which tests come on or off the list.
- When a change in challenge frequency was suggested, Ms. Yost reminded the Committee of the CLIA law which states PT “. . . shall be conducted on a quarterly basis, except where the Secretary determines for technical and scientific reasons that a particular examination or procedure may be tested less frequently.” Therefore, to change the frequency, scientifically sound reasoning and data must be provided to demonstrate the impact of the change on the accuracy of laboratory testing.

CLIAC Recommendations

- **There should be a defined list of analytes for which PT is required. If legally possible, those analytes should be separate from, but linked to, regulations, allowing the list to be more easily updated.**
- **Factors to be considered for adding required PT analytes to subpart I of the CLIA regulations should include:**
 - **Whether PT exists and material is available**
 - **The volume of testing for an analyte**
 - **Clinical relevance**
 - **Cost of adding an analyte**
- **The required number of PT challenges and frequency (five challenges, three times per year) should not be changed.**

Assessing Factors or Criteria

How should the factors or criteria for analyte inclusion be objectively assessed?

Committee Discussion

- Several members agreed with the Workgroup’s criteria and proposed adding analytes reported as part of a publically reported or mandated quality indicator to the list of clinical relevance components. The Chair cautioned that analytes may demonstrate variation in clinical relevance over time.
- Dr. Hearn commented that while PT results for some tests may indicate that laboratories are meeting current clinical goals, as clinical goals change, accuracy and precision may not be sufficient.

- Another member discussed the difficulty in determining which tests should be considered high risk, stressing every test result has a clinical consequence. A few members disagreed, noting a few tests are considered the mainstays of diagnosis. The Committee also discussed what would be the number of laboratories and/or volume needed to validate the existence of a particular test on the regulated list.
- A member emphasized PT is only one part of quality management and suggested keeping the list of regulated analytes at a minimum, requiring compelling clinical evidence that they make a difference to patient care.

CLIAC Recommendations

- **Inclusion Criteria for determining required PT analytes should be scientifically based.**
- **Criteria used to assess clinical relevance of an analyte should include consideration of:**
 - **Testing when a treatment decision is made solely on the result of that test**
 - **Tests that have critical values associated, i.e. results that require immediate communication with clinicians due to their life-threatening nature or serious risk to the patient**
 - **National practice guidelines that include testing the analyte**

Number of Analytes to Add

Should there be a reasonable limit on the number of analytes added to each new regulation published for proficiency testing?

Committee Discussion

This question was discussed in general but no recommendations were made.

Required PT for Other Specialties

Should PT be required for other specialties, such as histocompatibility or cytogenetics? If so, should factors similar to those listed in the first question be considered?

Committee Discussion

Several members concurred that every analyte which is moderate or high complexity should be assessed with traditional or alternative PT. The Chair stated in other specialties, such as histocompatibility and cytogenetics, alternative PT already exists, and it is allowed for in CLIA law.

No recommendations were made in response to this question.

Data for Analyte Inclusion

What data are needed to make decisions for inclusion of new analytes? What are sources for the data and how should CDC and CMS obtain and assess this data?

Committee Discussion

- A member commended staff on gathering and compiling data from various PT programs on test volumes and available analytes. The Chair remarked the issue is that there is no one source for overarching data. She noted that the Medicare data on test reimbursement covers many of the criteria the Workgroup examined when considering whether an analyte should be added to the list of regulated analytes.
- One member suggested that information be used in conjunction with the information from PT programs on available tests to build a list of regulated analytes.
- Another member added testing which appears in a nationally accepted practice guideline should be considered for inclusion.

No recommendations were made in response to this question.

Analytes for Consideration

Based on your experience, what analytes should have required PT?

Committee Discussion

- One member stated PT or alternative assessment should be required for all moderate or high complexity testing. The member suggested decreasing the burden by requiring PT be performed twice a year with flexibility in the number of challenges per event. Ms. Yost advised to change the frequency or number of challenges would require scientifically sound reasoning. Dr. Hearn pointed out that if the frequency were reduced, the number of samples in each event would most likely have to be increased.

CLIAC Recommendation

- **Ideally, every analyte should be assessed with traditional PT. If PT is not available, however, laboratories should continue to use alternative proficiency assessment as now required by CLIA.**

Impact of Additional Required PT

How would an expansion in the number of required analytes impact your laboratory or PT program?

Committee Discussion

- Ms. Yost noted accrediting programs already require PT on all testing performed in the laboratory, whether or not the analyte is considered regulated.
- Another member pointed out CLIA also requires laboratories to verify accuracy of tests twice per year utilizing voluntary PT for this purpose.

No recommendations were made in response to this question.

Process for Adding PT Analytes

Should there be a staging process for identifying analytes for which PT should be required but may not now be available?

Committee Discussion

- Several members recognized the need for a process to determine when and how analytes are added to the list and agreed a staging process should be instituted for implementing the requirement when practical. One member proposed a gated phase-in program that would separate the non-regulated analyte list into two categories: 1) analytes for which PT is currently offered less than three times per year, and 2) analytes for which PT is currently offered three times per year. The member commented that the addition of analytes in Category 2 to required PT should be fairly straightforward. Analytes in Category 1 could, perhaps, be offered by the PT programs within one to two years.
- Some members suggested that a staging list of potential new analytes should be a maintained when criteria are not yet clarified as to the number of available PT programs, number of laboratories performing the test, appropriate grading criteria, or there is inconclusive clinical relevance. When data are sufficient and the analytes are determined to be eligible for inclusion, they could be added.

CLIAC Recommendation

- **There should be a two-year phase-in period for implementation of required PT after adding analytes to the list.**

Deletion of Required PT Analytes

Should required PT for any of the analytes currently specified in subpart I be discontinued?

Committee Discussion

- A member suggested removing, from the regulated list, analytes for which ongoing PT is not adding much value. Another member noted there are a number of tests that laboratories continue to perform for which there are no clinical practice guidelines, and wondered if removal from the regulated analyte list would encourage laboratories to stop performing them.
- Another member suggested removing FDA classified Class 1 analytes which are well characterized, such as albumin or iron. Ms. Yost cautioned if the analyte is removed from the regulations, it is impossible for CMS to take action if a laboratory performs poorly for that analyte.

No recommendations were made in response to this question.

PT of the Total Testing Process

Could PT be improved to assess more steps in the total testing process?

This question was discussed in general but no recommendations were made.

Method Based PT

Would method-based PT be more appropriate for certain tests or analytes? What are the barriers to this approach?

Committee Discussion

- A member used cytogenetics as an example where method-based PT should be considered because PT cannot be provided for every translocation discovered in the laboratory.
- Method-based PT was also discussed by the Committee as a means to list required or regulated PT.

No recommendations were made in response to this question.

CLIA Proficiency Testing Criteria for Acceptable Performance

Rex Astles, Ph.D., DABCC, FACB

[Addenda K, L](#)

Lead, Proficiency Testing Team

Laboratory Practice Standards Branch

Division of Laboratory Science and Standards

Laboratory Science, Policy and Practice Program Office

Office of Surveillance, Epidemiology and Laboratory Services

Centers for Disease Control and Prevention

Dr. Astles began his presentation by referencing Subpart I §493.901 of the CLIA regulations regarding the requirements for PT programs. He noted when new analytes are added to the list of regulated analytes a criterion for acceptable performance would need to be established for each and the criterion would be applicable to all PT programs. Dr. Astles then discussed how the terms “target value” and “acceptance limits” relate to the concept of criteria for acceptable performance for both qualitative and quantitative tests. He provided examples of how the criteria for acceptable performance are outlined in the regulations and summarized the methods for establishment of target values in conjunction with the terms by which acceptance limits are specified. Dr. Astles concluded by reviewing the CLIA consensus requirements for PT scoring along with factors related to scoring considerations including matrix effects and ungradable challenges.

Workgroup Report - Criteria for Acceptable Performance and PT Sample Grading

James H. Nichols, Ph.D., DABCC, FACB

[Addendum J](#)

Professor of Pathology

Tufts University School of Medicine

Medical Director, Clinical Chemistry

Baystate Health

Dr. Nichols presented the next series of questions (slides 30-43) addressed by the Workgroup along with their input on the issues of:

- Criteria for acceptable performance for currently regulated analytes
- Criteria for acceptable performance for new quantitative analytes
- Determination of criteria for acceptable performance for qualitative tests
- Grading criteria
- Standardized PT scoring
- Matrix effects
- Ungradable challenges
- Peer group definition

Criteria for Acceptable Performance for Currently Regulated Analytes

Are the criteria for acceptable performance for the currently regulated analytes appropriate and which of the current criteria should be revised?

Committee Discussion

The Chair reminded the Committee acceptable performance is currently determined by standard deviations, fixed proportional limits as a percentage, or fixed concentration limits. Dr. Nichols mentioned the Workgroup contemplated the concept of partial credit, in which laboratories would not fail outright if they submit a partially correct answer. Several members supported the concept, while others thought it too difficult to standardize across programs. The Committee did not approve the suggestion for partial credit at this time but noted the concept for future consideration.

No recommendations were made in response to this question.

Criteria for Acceptable Performance for New Quantitative Analytes

How should criteria for acceptable performance be determined for quantitative tests or analytes that are added to the list of regulated tests?

Committee Discussion

- Several members expressed concern over the use of pass/fail rates as the criteria for acceptable performance because failing PT may not necessarily mean poor quality patient results. A member proposed evaluation of testing performance at clinical decision points. Another member raised the possibility of a laboratory failing at concentrations outside the clinically important (decision) range, but passing at the clinically relevant decision point, thus technically passing. Dr. Nichols asked if this implied that there should be double criteria for quantitative analytes added to the regulated list. He noted, in this circumstance, there would be one proficiency program for diagnostic criteria versus one for management criteria.
- Several members concurred that information gathered during the phase-in process for newly required PT should be used to scientifically establish grading criteria. During the phase-in, there should be enough time to perform PT and gather data so there

would be a scientific basis for establishing the grading criteria rather than arbitrarily selecting standard deviations or percentages for criteria for acceptable performance. At that time new analytes should be tested using different platforms and appropriate grading criteria could be established for each. They acknowledged this is complicated for the PT programs. Dr. Nichols reemphasized the concept of scientifically based grading criteria and questioned the need for a separate provision to re-evaluate currently required analytes for their appropriate clinical relevance.

CLIAC Recommendations

- **Grading criteria should be periodically reviewed for all analytes that require PT for continued clinical relevance or when relevant information becomes available.**
- **Information gathered during the phase-in process for newly required PT should be used to scientifically establish grading criteria.**

Determination of Criteria for Acceptable Performance for Qualitative Tests

For qualitative tests, should the criteria for acceptable performance be revised?

Committee Discussion

One member said if the laboratory reports qualitative results as positive, negative, or indeterminate, PT results should be reported in the same way. Several members agreed an indeterminate category should be considered for qualitative tests. Dr. Nichols added, for PT purposes, adding acceptable indeterminate categories would support the aforementioned partial credit suggestion.

CLIAC Recommendation

- **An indeterminate category should be considered an acceptable answer for certain analytes when this is normal practice.**

Grading Criteria

Should the criterion for determining the correct response by comparing the laboratory's response for each analyte with an established percentage of referee or participating laboratories be changed? Aside from blood banking, are the two options to determine the target value either by agreement with 80% of referee laboratories or by agreement with 80% of participants equally valid? Should one approach be preferred? If so, what would you suggest, and should it be required for scoring in all specialties and subspecialties?

Committee Discussion

- One member indicated if referee laboratories and peer groups utilized different methods, their results might differ because matrix effects may not be found in the referee group.
- To assess the two options of target value determination, several members proposed attempting to achieve 80% consensus by an all-method approach. For those analytes

already on the regulated list, the Chair suggested the PT programs determine consensus using the grading criteria in the regulations, and determine whether different methods can be aggregated or whether peer grouping by method is needed. A member emphasized that laboratories should not fail based on the fact that they are using a particular method that may have bias.

CLIAC Recommendation

- **Peer grouping should be retained when appropriate as a component of the grading criteria.**

Standardized PT Scoring

Are the current grading criteria sufficiently detailed and specific to assure standardized scoring by all programs?

Committee Discussion

Dr. Nichols stated the regulations should use a variety of fixed and proportional types of criteria based on the analyte and should assure that the criteria are clinically relevant.

No recommendations were made in response to this question.

Matrix Effects

To what extent does matrix effect limit the impact of PT by allowing peer-grouping? Does this occur often enough to warrant the addition of requirements for PT programs that would minimize the matrix effects within samples? What should these requirements be?

Committee Discussion

- Several members agreed PT material vendors need to assure that their samples perform appropriately with those testing systems used by their customers. Ms. Yost pointed out there is no formal authority overseeing PT material producers. She summarized the law, stating PT programs should distribute the samples using rigorous quality control to assure that the samples mimic actual patient specimens and the samples are homogeneous except for specific subspecialties such as cytology.

CLIAC Recommendation

- **All vendors involved in the production of PT material need to work to minimize matrix effects.**

Ungradable Challenges

What are the major reasons for ungradable challenges? Are there ways to minimize the number of ungradable results?

Should PT programs be expected to validate the stability and homogeneity of the samples they provide?

Committee Discussion

- A member indicated having fewer than 10 participants per challenge does not imply a sample problem. The member suggested two ungraded categories: one for too few participants, the other for sufficient participants but no consensus.
- The Committee recognized the current regulations require samples to be homogeneous and stable within the timeframe of analysis and this requirement should remain there.

CLIAC Recommendation

- **Designations for PT samples being ungradable (reason codes) should be clarified to distinguish between situations when there are too few participants to grade and sufficient number of participants but consensus is not reached.**

Peer Group Definition

Should “peer group” be defined in the regulations? Are there additional terms that need to be defined?

CLIAC Recommendation

- **Definition of the term “Peer Group” for possible inclusion in the regulations: A group of laboratories whose testing process utilizes similar instruments, methodologies, and/or reagent systems.**

Background - Microbiology PT Requirements

Roberta Carey, Ph.D.

[Addendum M](#)

Acting Director, Division of Laboratory Science and Standards
Laboratory Science, Policy and Practice Program Office
Office of Surveillance, Epidemiology, and Laboratory Services
Centers for Disease Control and Prevention

Dr. Carey presented the CLIA PT regulations for the microbiology specialty. She emphasized, unlike the other specialties, microbiology does not have analytes listed in the regulations. She provided information on the current regulatory requirements for each subspecialty: bacteriology, mycobacteriology, mycology, parasitology, and virology. Dr. Carey described the types of laboratories based on the types of services offered for each subspecialty designated in CLIA regulations Subpart I. She detailed the PT requirements for each subspecialty such as, number of samples per testing event, microorganism requirements of the PT sample, requirements for mixed cultures in the PT sample, antigen detection requirements, and susceptibility testing requirements. Dr. Carey concluded by describing the requirements for scoring microbiology PT samples and events.

Workgroup Report - Microbiology PT Requirements

Geraldine Hall, PhD, D(ABMM)
Section Head, Clinical Microbiology
Department of Clinical Pathology
Cleveland Clinic
Cleveland, OH

[Addendum N](#)

Dr. Hall began her presentation with a review of the issues facing microbiology PT such as the lack of a list of regulated analytes and the abundance of qualitative tests in microbiology. She presented the questions posed to the Workgroup concerning microbiology PT requirements, the Workgroup's comments, and their agreements. She stated that the microbiology Workgroup members agreed that all laboratories should be enrolled in and have acceptable performance on PT for all testing procedures performed for patient samples in their laboratory. Dr. Hall concluded by asking CLIAC to deliberate and make recommendations based on the Workgroup's agreements for regulatory revisions for the following:

- Levels of service
- Required categories of tests
- Major groups of microorganisms
- Emerging pathogens
- Patient histories
- Gram stain PT
- Mixed culture requirements
- Antimicrobial susceptibility testing
- Direct antigen testing
- Microbiology PT grading
- Monitoring performance over time
- Ungraded challenges

Committee Discussion

Ms. Passiment and the Committee commended Dr. Hall and the Workgroup members for their efforts in providing comments and reaching many agreements on the microbiology PT requirements. The Chair directed Committee members to discuss and make recommendations on each area of microbiology PT presented, focusing primarily on the PT Workgroup's agreement statements. The questions related to those areas are provided below, followed by points made during the discussion and CLIAC recommendations made.

Levels of Service

Have the levels of service or laboratory types listed in subpart I been of assistance to the PT programs when helping laboratories enroll properly or to surveyors in conducting laboratory inspections? If so, should they be retained or revised in any way?

Committee Discussion

There was discussion about how the Workgroup's questions and comments seemed to center on culture-based methods and appeared to exclude molecular methods for

microbiology PT. Dr. Hall clarified that the regulations for the five subspecialties in microbiology do not list methodologies, therefore all methods used for identification, including culture or molecular, are covered under the current regulations. She added that it was the Workgroup's intent to keep the regulations general to allow for all current and future testing methodologies. Dr. Hall stated the Workgroup agreements are focused on a need to maintain general levels of service in the regulations for each subspecialty.

CLIAC Recommendation

- **A system for categorizing levels of service must be maintained in the regulations to help laboratories determine what PT they need to perform and assist surveyors in monitoring PT performance and patient testing. Laboratories need to declare their patient reporting practices for organisms included in each PT challenge. However, PT programs may only gather this information as it is the inspecting agency's responsibility to review and take action if necessary.**

Required Categories of Tests

Should required categories of tests be specified for the microbiology subspecialties; for example, should microbiology PT be regulated based on sample source, complexity of testing, or another method?

Committee Discussion

- One member suggested inserting resistance testing and microbial identification into the proposed list of regulated microbiology tests suggested by the Workgroup.
- Another member requested clarification of the Workgroup's statement regarding the need to include a clear definition of which microbiology testing requires PT. The member asked if it was the Workgroup's intent to include some microbiology tests on a list. Dr. Hall responded that microbiology PT does not have regulated analytes; instead, PT is required for each subspecialty. Ms. Anderson added some laboratories may not clearly understand what PT they need to perform to achieve the overall subspecialty score; therefore, it would be helpful to laboratories if the regulations clearly stated what PT is required for each subspecialty.
- One member suggested removing the first Workgroup agreement statement by incorporating it into the second statement.

CLIAC Recommendation

- **The regulations need to include for all microbiology subspecialties, as applicable, stain(s), susceptibility and resistance testing, antigen and/or toxin detection, and microbial identification or detection.**

Major Groups of Microorganisms

Are the major groups of microorganisms listed for each microbiology subspecialty organized appropriately? For example, in bacteriology the major groups include anaerobes, Enterobacteriaceae, Gram-positive bacilli, Gram-positive cocci, Gram-

negative cocci, and miscellaneous Gram-negative bacteria.

If so, how can we ensure the laboratories are adequately challenged over time with each of the major groups for a subspecialty?

If not, is there a better way to categorize the microorganisms that should be included in a PT program over time?

Should the specific lists of example organisms be retained?

Committee Discussion

A member questioned if the list of organisms in each subspecialty needed to be added to the recommendation, such as cestodes, nematodes, and amoebas for parasitology. Dr. Hall and Dr. Carey clarified that the regulations should include a generic list of organisms for each subspecialty; the Workgroup's comment provided the bacteriology groups as an example.

CLIAC Recommendation

- **Require PT for a generic list of organisms in each subspecialty. For example, in bacteriology the groups listed should include Gram-negative bacilli, Gram-positive bacilli, Gram-negative cocci, and Gram-positive cocci.**

Emerging Pathogens

Should PT programs be required to offer microorganisms known as common and newly emerging pathogens for a particular sample source?

How can we maintain flexibility and keep the program relevant with respect to including new and emerging pathogens and technologies, keeping up with reclassifications and name changes, and describing the appropriate organisms to be included in PT over time?

Committee Discussion

Dr. Hearn commented that during the September, 2005 CLIAC meeting he presented information and suggestions from the June 14, 2005, meeting that was held to address PT for infectious disease agents. The PT experts and stakeholders at that meeting suggested that each year PT programs provide CDC with proposed PT content for microbiology samples containing potentially infectious organisms to determine their acceptability for shipping and testing in clinical laboratories. They also suggested that once PT samples are prepared, PT programs should verify composition of PT sample contents before shipping. Dr. Hearn noted that the Workgroup did not present any agreements on this topic. Dr. Hall commented that the Workgroup discussed PT sample safety issues but did not suggest any agreements be brought forward to CLIAC on the topic. Dr. Carey added that the Workgroup did not specifically address safety issues around microorganisms used in PT samples, and agreed PT programs should have practices in place to address those issues.

Patient Histories

Should PT programs be required to provide specific elements of a patient history, or sample information needed for laboratories to process and handle PT samples appropriately (as patient samples would be handled)?

Committee Discussion

One member commented that the source of the sample is needed to determine which culture media to use. If the source is not indicated, the sample will have to be cultured on many types of media and PT would become very costly. Dr. Hall clarified by explaining that the intent of the Workgroup was to prevent laboratories from excluding themselves from PT because they do not perform testing on samples from certain sources. She said that in many cases the history will describe the symptoms which will lead to the proper media selection. Dr. Hall suggested adding verbiage to the Workgroup agreement that source information be provided with an emphasis that the source information should not keep a laboratory from performing PT on that sample.

CLIAC Recommendation

- **For PT, patient histories and source should be provided, however this information should not preclude the laboratory from performing PT.**

Gram Stain PT

Should required PT for Gram stains include organism morphology?

Should direct specimen Gram stains include additional host elements (e.g. cells, mucus)?

Committee Discussion

The Chair questioned if the Workgroup's statement about including stain reaction and morphology pertained to PT samples or results. Dr. Hall clarified the statement indicating that both stain reaction and morphology should be included in the PT results for Gram stain.

CLIAC Recommendation

- **PT results for Gram stains should include both stain reaction and morphology.**

Mixed Culture Requirements

Is the current 50% mixed culture requirement appropriate?

CLIAC Recommendation

- **Lower the mixed culture requirement from 50% to 25% for PT challenges of both sample types (those that require laboratories to report only the principal pathogen and those that require laboratories to report all organisms present).**

Antimicrobial Susceptibility Testing

Should the required PT for bacteriology antimicrobial susceptibility testing (AST) be revised in any way?

Committee Discussion

- One member asked if the Workgroup intended to limit PT requirements to only *in vitro* phenotypic susceptibility or should resistance testing also be considered. Dr. Hall responded the Workgroup had focused on *in vitro* susceptibility testing but the CLIAC recommendation would not need to be limited to that.
- Dr. Carey stated that under the current regulations, AST PT on a Gram-positive or Gram-negative organism may occur as infrequently as once per year. By increasing the frequency of susceptibility PT challenges and requiring one Gram-positive and one Gram-negative organism per event, potential issues with susceptibility testing within a laboratory could be detected sooner. The Chair suggested including susceptibility and/or resistance testing to the requirement.
- A member suggested incorporating clinical relevance into the recommendation. Another member responded that a recommendation had already been made relating to clinical relevance in the Analyte Inclusion/Prioritization and Grading Criteria general Workgroup section which should apply to all areas of PT.

CLIAC Recommendation

- **Required PT for antimicrobial susceptibility and/or resistance testing should be increased to two challenges per event for a total of six challenges per year in bacteriology and should include one Gram-positive and one Gram-negative organism in each event.**

*Should PT be required for susceptibility testing in mycology, virology, or mycobacteriology for organisms other than *M. tuberculosis*? If so, what should it include?*

Committee Discussion

- One member stated that if a laboratory is performing testing and reporting results on susceptibility tests other than bacteriology, then they should be performing PT on those tests. Dr. Carey agreed that the intent of the Workgroup was to require PT for all patient testing performed by a laboratory.
- For consistency, Ms. Anderson suggested adding resistance testing to the requirement. A member questioned if this recommendation would apply to resistance testing such as HIV-1 antiviral resistance testing by sequencing. Dr. Hall verified that resistance testing is covered in the recommendation.

CLIAC Recommendation

- **PT should be required for laboratories that perform susceptibility and/or resistance testing in all microbiology subspecialties. It should include two challenges per event for a total of six challenges per year and should include resistant organisms.**

Direct Antigen Testing

Direct antigen testing is only included in bacteriology and virology. Should it be included in other microbiology subspecialties to require PT in those areas as well?

Committee Discussion

One member commented that recently the influenza direct antigen test was shown to have low sensitivity. The member voiced concern over encouraging laboratories to use antigen tests which may have sensitivity and specificity issues. Dr. Carey clarified that many laboratories only perform antigen testing. The Workgroup's intent was to require PT in areas currently not regulated such as parasitology where direct antigen testing is being performed and reported on patient samples.

CLIAC Recommendation

- **PT for direct antigen testing should be required for all subspecialties.**

Microbiology PT Grading

How can the microbiology grading requirements be clarified so that grading is more standardized and applied fairly?

CLIAC Recommendation

- **Retain the five required challenges per event and 80% required consensus for grading.**

Monitoring Performance Over Time

Since microbiology does not have analytes, should changes be made to microbiology PT grading to allow for monitoring performance over time on a particular test or examination – i.e. Gram stain, culture, or susceptibility testing?

Committee Discussion

- For consistency, the Chair suggested inserting resistance testing and microbial identification into the proposed list of regulated microbiology tests that will require the reporting of an individual score.
- Dr. Carey clarified the requirements for microbiology score reporting. She stated that laboratories receive a score from their PT program for the individual PT tests they perform. The scores on the individual tests are then combined into an overall composite score for that subspecialty and reported to CMS. Ms. Anderson added that during the Workgroup discussions, accreditation agencies mentioned that due to the rolling up of individual scores into a composite score, they sometimes have difficulty determining problematic testing areas within a microbiology laboratory.

CLIAC Recommendation

- **All PT programs should be required to provide CMS with the overall score for each subspecialty, with a line item underneath that includes a score on**

the individual PT tests or procedures that comprised the subspecialty score - such as stain(s), susceptibility and resistance testing, antigen and/or toxin detection, and microbial identification and detection.

Ungraded Challenges

Should challenges be ungraded when laboratories fail to identify the target(s) if PT programs can demonstrate they provided quality samples?

What are the major reasons for ungraded challenges?

Should PT programs resend ungraded challenges and monitor performance over time?

No recommendations were made in response to these questions since ungradable challenges had been addressed during the general PT discussion.

Workgroup Report - PT Referral

James Nichols, Ph.D., DABCC, FACB
Professor of Pathology
Tufts University School of Medicine
Medical Director, Clinical Chemistry
Baystate Health

[Addendum J](#)

Dr. Nichols began his presentation (slides 45-52) with an overview of the CLIA law 42 U.S.C §263a(i)(4), Improper Referrals. The law requires stringent penalties for intentional PT sample referral to another laboratory for analysis. Dr. Nichols stated CMS had reviewed 14 cases of PT referral. Seven cases resulted in a one year revocation of each CLIA certificate. Additionally the laboratory directors were barred from directing a laboratory for two years. Five cases resulted in less stringent sanctions, and two cases are currently being reviewed. He touched on some of the areas of confusion caused by the existing CLIA regulations such as: PT samples must be tested as patient samples, but must not be sent to another laboratory for testing; situations where laboratories in a single organization with multiple CLIA certificates are considered multiple laboratories; and viewing results from another laboratory is considered PT referral even if those results are not reported. Dr. Nichols presented the Workgroup's comments on PT referral which included other examples of inadvertent PT referral and suggestions to allow PT referral in certain cases, such as when a test is needed in order to report the complete result. Due to instances when the PT referral was not intentional but due to a lack of understanding of the law, Dr. Nichols stated that CMS has requested assistance with the definition of "intentional PT referral" and needs suggestions for regulatory language that would allow more flexibility and discretion while still adhering to the law.

Committee Discussion

Ms. Passiment directed the Committee to address the dilemma CMS faces with PT referral. She presented examples of unintentional PT referral such as, a laboratory's protocol may indicate that patient samples are to be referred to another laboratory for confirmation or to perform a certain part of a test to achieve a complete result. A

different type of PT referral could also result when the same person works in multiple laboratories and may encounter identical PT samples and the results at the different locations.

How can the current regulatory language be changed to allow CMS flexibility and discretion, yet still conform to the statutory requirement for PT referral?

Committee Discussion

- One member asked how large commercial laboratories handle PT samples that are sent to them from other laboratories for testing. Ms. Yost responded that they contact CMS to inform them of the PT referral. CMS then contacts the sender laboratory to address the issue. The member suggested laboratories only perform PT on the tests they perform in the laboratory. If there is any additional testing or part of a test that is normally referred, the laboratory should indicate it on the PT results form. Ms. Yost commented that is the current PT testing procedure, but this procedure limits the laboratory's ability to analyze the PT results as it would a patient sample due to the lack of testing results from tests that are referred. She added it is sometimes difficult to determine "intent."
- A member suggested a system allowing PT referral testing on those tests that a laboratory does not perform itself, but the results of which are imperative for final result interpretation. Another member agreed and suggested a form on which the laboratory would indicate its procedure for this type of test and could reference the CLIA certificate number of the laboratory where the PT sample was sent to complete testing. CMS, surveyors, and other partner laboratories would be able to review the supporting documentation to assure the PT referral was necessary to complete the result.
- A member expressed concern about the larger laboratories receiving many PT samples for referral testing while also having to perform PT on those same samples for their laboratory. Another member added that the laboratory where the samples are sent for testing should have a document stating that they are testing the PT samples as referred and should not be penalized for the referral testing. The referral laboratory should have procedures in place for its own PT testing.
- One member remarked the laboratories that should be punished are the laboratories that intentionally send PT samples to other laboratories for testing instead of running the samples themselves. Several members agreed that the "intent to defraud" statement needs to be clarified.
- One member suggested providing examples of acceptable PT referral. The Chair responded that the language in the regulations should be kept in a general context due to the fact that some PT referral exceptions could be missed. Ms. Yost suggested providing a list of acceptable PT referral situations in the Interpretive Guidelines.

CLIAC Recommendations

- **Distinguish acceptable "PT referral" from unacceptable PT referral with the "intent to defraud" in regulations at §493.801(b)(4) allowing CMS more flexibility in imposing sanctions on laboratories.**

- **Designation of acceptable PT referral would allow laboratories to treat PT exactly as patient samples and perform reflex or referral testing when it is included in their standard procedure for patients.**
- **Laboratories should provide documentation to the referral laboratory on the nature of the referral. Referral laboratories should not be penalized.**

Public Comments

[Addenda O, P, Q, R](#)

ADJOURN

Ms. Passiment acknowledged the CDC staff that assembled the meeting agenda and provided meeting support, and thanked the CLIAC members and partner agencies for their support and participation.

Ms. Passiment announced the next CLIAC meeting would be March 2-3, 2011 and adjourned the Committee meeting.

I certify this summary report of the September 1-2, 2010 meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

Dated 11/22/2010