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NEW/REVISED MATERIAL--EFFECTIVE DATE: February 13, 2004

This material was rewritten due to publication of CMS-2226-F; 42 CFR 493 Medicare, Medicaid, and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; Final Rule on January 24, 2003, with an effective date of April 24, 2003.

NOTE: The attached document will replace the current Publication 7, Appendix C, Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services. The new document is in the new CMS format for Interpretive Guidelines and is formatted for Web-based purposes.

APPENDIX C

SURVEY PROCEDURES AND INTERPRETIVE
GUIDELINES FOR LABORATORIES
AND LABORATORY SERVICES

(Rev. 32, 02-13-2004)

Appendix C

Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services

The items listed below replace the current Publication 7, Appendix C, Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services. This material was rewritten due to publication of CMS- 2226-F: 42 CFR 493 Medicare, Medicaid, and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; Final Rule on January 24, 2003, with an effective date of April 24, 2003.

1. [Policy for Conducting Surveys](#)
2. [Index and Subparts A-H \[General Provisions, Certificates and Proficiency Testing\] of the CLIA regulations - Sections 493.1 through 493.865](#)
3. [Subpart J](#) [Facility Administration] - Sections 493.1100 through 493.1105
4. [Subpart K, Part 1](#) [Quality System for Nonwaived Testing; General Laboratory Systems, Preanalytic Systems & Analytic Systems (general requirements)] - Sections 493.1200 through 493.1256
5. [Subpart K, Part 2](#) [Quality System for Nonwaived Testing; Analytic Systems (specialty and subspecialty requirements) and Postanalytic Systems] – Sections 493.1261 through 493.1299
6. [Subpart M](#) [Personnel] - Sections 493.1351 through 493.1495
7. [Subpart Q](#) [Inspection] - Sections 493.1771 through 493.1780

SURVEY PROCEDURES AND INTERPRETIVE GUIDELINES
FOR LABORATORIES AND LABORATORY SERVICES

POLICY FOR CONDUCTING SURVEYS

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Interpretive Guidelines for Laboratories and Laboratory Services

POLICY FOR CONDUCTING SURVEYS

Survey protocols and interpretive guidelines are established pursuant to pertinent sections of the Social Security Act, the Public Health Service Act, the Clinical Laboratory Improvement Amendments (CLIA) of 1988, and the CLIA regulations at 42 CFR Part 493 to provide guidance to personnel conducting surveys of laboratories. The protocols and guidelines clarify and/or explain the Federal requirements for laboratories and are required for use by all surveyors assessing laboratory performance based on these Federal requirements. The same survey protocols are used by the regional office (RO) and/or State Agency (SA) surveyors.

The following protocols represent an outcome-oriented method to be used to conduct the survey. The focus of the survey is to assess how the laboratory monitors its operations and ensures the quality of its testing. The intended use of these protocols is to promote consistency in the approach to the survey process, and to ensure that a laboratory's operations are reviewed in a practical, efficient, and effective manner so that at the completion of the survey there is sufficient information to make compliance determinations. While the purpose of the protocols and guidelines is to provide direction in preparing for the survey; in conducting the onsite survey; and for analyzing, evaluating, and documenting survey findings; the surveyor's professional judgement is the most critical element in the survey process.

CMS' objective is not only to determine the laboratory's regulatory compliance but also to assist regulated laboratories in improving patient care by emphasizing those aspects of the regulatory provisions that have a direct impact on the laboratory's overall test performance. CMS promotes the use of an educational survey process especially on initial laboratory inspection to help laboratories understand and achieve the quality system concepts. It is the surveyor's objective, using professional judgement, to determine, based on observation of the laboratory's (past and current) practices, interviews with the laboratory's personnel, and review of the laboratory's relevant documented records, whether it is producing quality test results (i.e., accurate, reliable, and timely). The primary objective of the survey process is to determine whether or not the laboratory meets the CLIA requirements. The surveyor meets this objective by employing an outcome-oriented survey process or approach, the intent of which is to focus the surveyor on the overall performance of the laboratory and the way it monitors itself, rather than on a methodical evaluation of each standard level regulatory requirement.

Surveyors must make every effort to minimize the impact of the survey on laboratory operations patient care activities, and to accommodate staffing schedules and departmental workloads as much as possible. In facilities providing direct patient care, e.g., physician offices, clinics, residential care facilities, and hospitals, surveyors must avoid interrupting or interfering with patient care. Surveyors must respect patient privacy and confidentiality at all times in all survey settings.

Provider-Performed Microscopy (PPM) procedures are moderate complexity tests subject to routine biannual surveys except when the laboratory holds a certificate for PPM procedures.

When performing a survey on a facility that conducts PPM procedures, the appropriate requirements at 42 CFR Part 493, Subparts C, H, J, K, M, and Q apply. (Refer to Section IX for information concerning conducting surveys of laboratories holding a certificate for PPM Procedures.)

For information concerning conducting surveys of waived testing, refer to Section IX.

THE OUTCOME-ORIENTED SURVEY PROCESS

The principal focus of the outcome-oriented survey is the effect (outcome) of the laboratory's practices on patient test results and/or patient care. The outcome-oriented survey process is intended to direct the surveyor to those requirements that will most effectively and efficiently assess the laboratory's ability to provide accurate, reliable, and timely test results.

In the outcome-oriented survey process, the surveyor reviews and assesses the overall functioning of the laboratory and evaluates the laboratory's ability to perform quality testing; that is, the surveyor evaluates the laboratory's quality system. The quality system requirements in the Introduction to Subpart K and the General Laboratory, Preanalytic, Analytic, and Postanalytic Quality Assessment requirements are appropriate guides for the surveyor to organize the review.

In the outcome-oriented survey process, emphasis is placed on the laboratory's quality system as well as the structures and processes throughout the entire testing process that contribute to quality test results. The surveyor selects a cross-section of information from all aspects of the laboratory's operation for review to assess the laboratory's ability to produce quality results. The surveyor reviews the cross-section of information to verify that the laboratory has established and implemented appropriate ongoing mechanisms for monitoring its practices, and identifying and resolving problems effectively.

If the findings from the review of the laboratory's ongoing mechanisms for ensuring quality test results are sufficient to make the determination of compliance and if the evaluation does not warrant a more in-depth review, the surveyor concludes the survey and asks if the laboratory has any questions about CLIA requirements.

Note: Although Appendix C, Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services, includes guidelines and instructions for each regulatory requirement and encompasses all types of laboratory facilities, use only those portions applicable to the laboratory operations and complexity of testing performed.

I. IDENTIFYING SOURCES OF INFORMATION

A. Scheduling Surveys.--For efficiency when scheduling, attempt to cluster surveys geographically. Schedule the recertification survey at least 6 months prior, but no earlier than 12 months prior to the expiration of the laboratory's current certificate. In order to permit observation of actual testing during the initial survey, schedule the initial survey at least 3 months after the laboratory opens. Any new laboratories, and if at all possible, complaint and validation surveys in the geographic area should be worked into the survey schedule. Extenuating circumstances require RO review.

Establish a date and time for the survey once the schedule has been completed. If a laboratory operates more than one shift or location, schedule survey hours to include a representative cross-section of shifts or locations, as necessary.

To enhance survey effectiveness and efficiency, except in the case of complaints, consider mailing the following forms to the laboratories before the scheduled survey date. Request the laboratory complete the forms and either return them to the SA or hold them for review during the onsite survey.

- o Disclosure of Ownership and Personnel and Control Interest statement. Collect on initial survey and with change of ownership. (Refer to the State Operations Manual (SOM) Chapter 2, §2005.) Consult the annual laboratory registry or CLIA/Online Survey Certification and Reporting (OSCAR) database to assist with determining whether the owner has had a laboratory certificate revoked within the last 2 years;

- o Laboratory Personnel Report (CLIA), Form CMS-209 (required) with directions for completing or updating information, adding new personnel or changes in positions or status; and

o Clinical Laboratory Improvement Amendments (CLIA) Application for Certification, Form CMS-116 (required) with signature of current owner/operator/director; (Refer to Section IX Additional Information for counting test volumes).

Request the following information be accessible and retrievable at the time of survey:

- o Standard operating procedure manual with all test procedures (e.g., package inserts and supplemental information, as necessary);
- o Reference laboratories' client services manual, if applicable;
- o Records of tests referred to other laboratories;
- o Personnel records, including:
 - Diplomas, certificates, degrees;
 - Training, and experience;
 - Continuing education;
 - Competency assessment;
 - Duties/responsibilities; and
 - Personnel changes.
- o Quality control records, including:
 - Remedial action information;
 - Calibration and calibration verification records;
 - Statistical limits; and
 - Instrument maintenance and function checks records.
- o Proficiency testing (PT) reports, including:
 - Test runs with PT results;
 - Direct printouts; and
 - Remedial actions for unsatisfactory results.
- o Quality system assessment plan and documentation;

For each of the systems:

- policies and procedures to monitor, assess, and correct identified problems;
- documentation of ongoing assessment activities, including
 - review of the effectiveness of corrective actions taken
 - revision of policies and procedures prevent recurrence of problems; and
 - discussion of assessment reviews with staff.
- o Safety information; and
- o Patient testing records:
 - Requisition (patient charts may be used);
 - Work records (direct printouts); and
 - Patient test reports (patient charts may be used).

B. Announced and/or Unannounced Surveys.--Section 353(g)(1) of the Public Health Service Act provides for either announced or unannounced surveys. Complaint or revisit surveys must be conducted on an unannounced basis. (Refer to the SOM, Chapter 6, §6106 for policy regarding announced and/or unannounced surveys. For announced surveys, allow up to four-weeks notice.) When applicable, the laboratory may be notified by telephone or mail. Notification may include the actual date and time of the survey. For either an initial CLIA or

recertification CLIA survey, an unannounced survey may be performed after one appointment is cancelled by the laboratory. The laboratory must be informed of this when originally notified about the survey. Request that the laboratory notify the RO or SA, as appropriate, if its laboratory operations are not conducted during usual hours of operation or only on specific days and times. Surveys are to be conducted during the laboratory's routine hours of operation. Confirm the laboratory's certificate type and advise the laboratory to notify the SA of any changes that would necessitate a different certificate. If the laboratory has applied for a certificate of accreditation, ask the laboratory to provide documentation (e.g., written verification from the accreditation organization) of its accreditation status.

C. **Pre-Survey Preparation**--Prior to each survey, review the laboratory's file, including the CLIA-database information. To determine the size of the survey team and the expected time required for the survey, consider the number of sites under the certificate, the scope and volume of testing, and the test complexity.

1. **Personnel**--Include the completed or updated Form CMS-209 in each survey package. Use this information during the onsite survey to evaluate positions currently held by employees in accordance with the requirements. Focus on new personnel since the last survey.

2. **Services Offered**--Review the CLIA application, the list of tests and specialties/subspecialties, and any correspondence from the laboratory to determine the complexity of tests performed. Ascertain whether the laboratory has changed complexity of testing, specialties/subspecialties, added/deleted tests or services, since the last survey.

3. **PT**--Review PT records to ensure that the laboratory is enrolled and participating in an approved program for each PT regulated analyte, specialty, and subspecialty for which testing is performed. Note any unacceptable, unsatisfactory, or unsuccessful scores and any analyte, specialty, and/or subspecialty that are not evaluated by the proficiency testing program provider. Use this information to target particular tests for review during the survey.

4. **File Review**--Evaluate the laboratory's ability to maintain compliance between surveys by reviewing its file for:

- o Previous survey results and plans of correction, noting patterns, number, nature of deficiencies, and dates of correction;

- o Enforcement action(s) taken or in progress, e.g., limitations of the certificate or voluntary withdrawal of a specialty, subspecialty, or analyte/test due to unsuccessful proficiency testing or loss of qualified personnel; and

- o Complaint allegations noting frequency, significance, severity and, if substantiated, the resolution.

II. ENTRANCE INTERVIEW

The entrance interview sets the tone for the entire survey. Be prepared, positive, courteous, and make requests, not demands. Upon arrival, present the appropriate identification, introduce other team members, inform the facility's administrator, director, or supervisor of the purpose of the survey, the time schedule, and explain the survey process. Identify a contact person and establish a communication level based on the degree of technical knowledge of the contact person.

If the laboratory consists of multiple testing sites, verify all information concerning testing performed at each site. If one or more sites do not meet the multiple site exceptions in the regulations (42 CFR §§493.35(b), 493.43(b) and 493.55(b)), explain the reason and have the owner/operator/director complete Form CMS-116 for each applicable site. (Refer to Section IX for information concerning conducting surveys of multiple testing sites under one certificate.)

Inform the laboratory that the survey will include a tour of the facility, record review, observation, and interviews with personnel involved in the pre-analytic, analytic, and post-analytic phases of the testing process. Establish personnel availability and discuss approximate time frames for survey completion. Determine whether the deficiencies, when identified, are to be discussed with testing personnel, and explain that an exit conference may be held to discuss survey findings. Refer to the SOM, Chapter 6, §§6124 and 6126 for additional information regarding the exit conference.

Request that the laboratory collect any documents, records, or information that may be needed to complete the survey, and solicit and answer any questions the laboratory may have concerning the survey process.

III. INFORMATION GATHERING

The technique for information gathering includes observation, interviews, and record review and these are usually performed concurrently. The information gathering process is critical in the determination of quality laboratory testing. Gather sufficient information to evaluate the laboratory's operations without being overly intrusive or gathering excessive information. As each laboratory is unique in the services offered, the order of gathering information may be different for each survey. The timing for observing testing and the availability of staff for interview may determine the sequence of the survey.

Consider the laboratory's compliance history (deficient practices and Plans of Correction). Verify the correction and continued compliance with all previously cited deficiencies. Pay particular attention to deficiencies that the laboratory has failed to correct. Refer to enforcement requirements the 42 CFR Part 493, Subpart R, if needed.

A. Organizing the Survey.--Consider the following variables when making determinations for organizing the survey and the areas to be reviewed:

- o Purpose of the Survey:
 - Initial or recertification (Refer to SOM Chapter 6, §§6112-6114 regarding CLIA recertification using the Alternative Quality Assessment Survey (AQAS));
 - Complaint;
 - Follow-up; and/or
 - Validation.
- o Pre-survey Information:
 - Problematic PT;
 - Previous survey deficiencies;
 - Complaints; and/or
 - Enforcement actions.
- o Size and Organization of the Laboratory:
 - Type of instruments/test procedures;
 - Type of information system(s);
 - Number of supervisors and testing personnel;
 - Number of testing sites;
 - Scheduling of testing (e.g., Stat, daily, weekly shifts);
 - Number of specialties/subspecialties;
 - Test volume;
 - Record availability; and/or
 - Type of patients/clients served.

B. Observation of Facilities and Processes.--Observe the laboratory's physical layout. These observations should include specimen collection and processing, "prep" and clean-up areas, testing and reporting areas, and storage areas. Whenever possible, observe specimen processing and test performance, noting information which would precipitate

revisiting an area, interviewing personnel, or requesting records for review. Observe and verify that reagents, kits, and equipment correlate with test menu, clients served and results reported. Also observe whether staffing appears adequate for test volume. Schedule the survey date/time to observe personnel performing specimen processing, testing, and reporting of results in each specialty/subspecialty of service. If it is not possible to observe testing, ask for a verbal walk-through of the procedure. Do not distract staff when observing operations and personnel activities.

Focus observations on:

- o Specimen integrity;
- o Quality control performance;
- o Skills and knowledge of personnel regarding:
 - Performance of testing;
 - Evaluation of test results;
 - Identification and resolution of problems; and
- o Interactions of personnel regarding:
 - Availability of supervisor to staff; and
 - Communication among personnel.

At all times respect patient privacy and do not interfere with patient care and confidentiality.

C. Interviews.--Interview staff to confirm observations and obtain additional information, as necessary. Obtain information to identify personnel interviewed, such as name or code. Ask open-ended questions, e.g., probes from the guidelines, and if necessary, repeat or restate the response given by the staff to confirm what was said.

During the interview of personnel, evaluate their knowledge and skills for performing tests, identifying problems and the methods for corrective and remedial actions. Interviews should include as many staff members as necessary to form a judgement as to the ability of staff to perform their duties. Handle all staff or individual allegations of problems as complaints. Determine, as best as possible, the validity of the allegations prior to leaving the laboratory. Do not cite deficient practices or complaints based on allegations without verification. Conduct a follow-up investigation, if appropriate, of serious allegations or complaints that cannot be substantiated during the present survey, e.g., falsified test results or referral of PT specimens to another laboratory for testing.

D. Record Review.--Gather relevant information that will reflect the laboratory's ability to provide quality testing from all areas of the laboratory including records encompassing the time period since the last certification survey. Determine all new tests, new test methods, and new equipment added since the prior survey and review documentation relevant to as many of these factors as possible when reviewing laboratory records. The amount of records selected and reviewed is not intended to be statistically valid, but rather a representative cross-section of various records. Avoid predictable patterns of gathering information (e.g., same tests or time periods). Do not allow the laboratory to select the records for review. Consider the types of clients and/or facilities that the laboratory serves, e.g., nursing homes, pediatric, dialysis units, public health clinics, cancer clinics, and routine physicals. Choose a variety of patient records across the laboratory's spectrum of clients. When test information must be gathered from medical records, be considerate when handling these records, as they contain confidential information. If possible, review medical records in the presence of office or laboratory personnel and with consideration to confidentiality.

Subpart K delineates the laboratory's responsibility for performing its own internal reviews. This is an excellent starting point for an outcome-oriented survey. Review a cross-section of information selected from records of quality system assessment activities within each of the four systems. Review a cross-section of information simultaneously assessing the laboratory's

ability to provide quality test results as well as its ability to identify and correct problems. Refer to the quality system assessment portions of the regulations as a guide for organizing your selection and review of information to assess the laboratory's overall compliance. Investigate further any problems identified but not addressed by the laboratory's quality system assessment. If the laboratory is failing to monitor (or effectively monitor) its own system and correct its problems, you can direct the laboratory to the requirements and the relevant sections for its particular setting.

Make copies of any records needed to support deficient practices.

Assure that reviews of PT (Subpart H), Facility Administration (Subpart J), Quality System (Subpart K) and Personnel (Subpart M) include the following:

1. PT--Verify the laboratory is appropriately enrolled and participates in a CMS approved PT program(s) for each specialty, subspecialty, analyte, and/or test for the entire period of time the laboratory has been performing testing for each regulated test (not just shortly before the survey).

If the laboratory has unacceptable analyte/test results or unsatisfactory performance in specialties or subspecialties since the last survey, review the specific record, corrective action, and any other data such as education and training of staff associated with PT remediation. Include both patient test results and QC records which were assayed in the same run as the failed PT in the review. In addition:

- o Verify that the laboratory has reported results under the appropriate methodology/instrumentation used for test performance, e.g., automated vs. manual hematology;

- o Verify that the laboratory did not engage in inter-laboratory communications and/or refer its PT samples for testing prior to reporting results to the PT provider;

- o Verify that PT samples were handled, prepared, processed, examined, tested, and reported, to the extent practical, in the same manner as patient samples; and

- o For tests where there is no PT available and/or those tests performed by the laboratory that are not included in subpart I, determine that the laboratory verifies the accuracy of each test at least twice a year.

2. Facility Administration--Review records for the appropriate retention times and assure the laboratory adheres to appropriate safety, arrangement, space, ventilation, and contamination procedures. If the facility provides transfusion services, verify that the arrangement is current, the blood products are stored appropriately, and transfusion reactions are investigated and reported to the appropriate authorities in a timely manner.

3. Quality System--General Laboratory, Preanalytic, Analytic, and Postanalytic System Quality Assessment--Using the patient test requisitions, test records, test results, and test reports or, as applicable, patient charts, review all phases of the laboratory testing processes, including instructions for specimen storage. If possible, when reviewing individual patient test results, correlate test requisition(s) or medical record information with final report(s). Refer to Postanalytic Systems Quality Assessment for guidance in reviewing and correlating patient test results. After determining the patient population serviced by the laboratory, e.g., geriatrics, public health clinics, dialysis units, health fairs, and hospitals, review the following:

- o A cross-section of patient test results encompassing all specialties and subspecialties of testing performed in the laboratory in sufficient numbers to determine if results vary significantly from expected population norms;

- o Worksheets or instrument printouts, looking for outliers, trends, etc., when tests are performed in batches;

- o Several worksheets, instrument printouts, or medical records over time for tests performed at random;
- o Test results that are disproportionately abnormal or normal; and
- o The correlation of initial test results and/or test result of various analytes of a patient over time.

Review QC practices and evaluate whether the laboratory is following its own QC protocols or those procedures specified by the manufacturer. Review QC results, including outliers, shifts, trends, and corrective actions taken, when necessary.

Refer to the establishment and verification of performance specifications at 42 CFR Part 493.1253 for guidance in reviewing the laboratory's policies and criteria for adding a new method, test system or analyte to its test menu.

Correlate reported patient test data with QC data and/or quality systems assessment records to ensure proper performance and documentation of controls. Review original test data (instrument printouts or computer files). Verify that patient results have not been reported when QC data was unacceptable according to the laboratory's protocol.

Consider the following in relation to the laboratory's patient population:

- o New methodologies and equipment;
- o QC and calibration materials used;
- o Source and availability of QC limits;
- o Evaluation and monitoring of QC data; and
- o Corrective action for QC failures.

4. Personnel.--The scope of the review of personnel records (qualifications, training, and competency) will be related to the type of survey, type and complexity of testing performed, and the observations and findings of the survey. For initial CLIA certification surveys, evaluate the qualifications and experience of the laboratory director and each technical consultant, technical supervisor, clinical consultant, general and cytology supervisor, and cytotechnologist. Evaluate the qualifications and experience of a cross-section of testing personnel.

For CLIA recertification surveys, it is not necessary to review personnel records of individuals previously evaluated unless there have been changes in the individual's position and/or the laboratory's test menu since the last survey. Focus on any new laboratory director, technical consultant, technical supervisor, clinical consultant, general and cytology supervisor, cytotechnologist, and testing personnel. Refer to Subpart M for additional information concerning personnel training, experiences, competency, and qualifications.

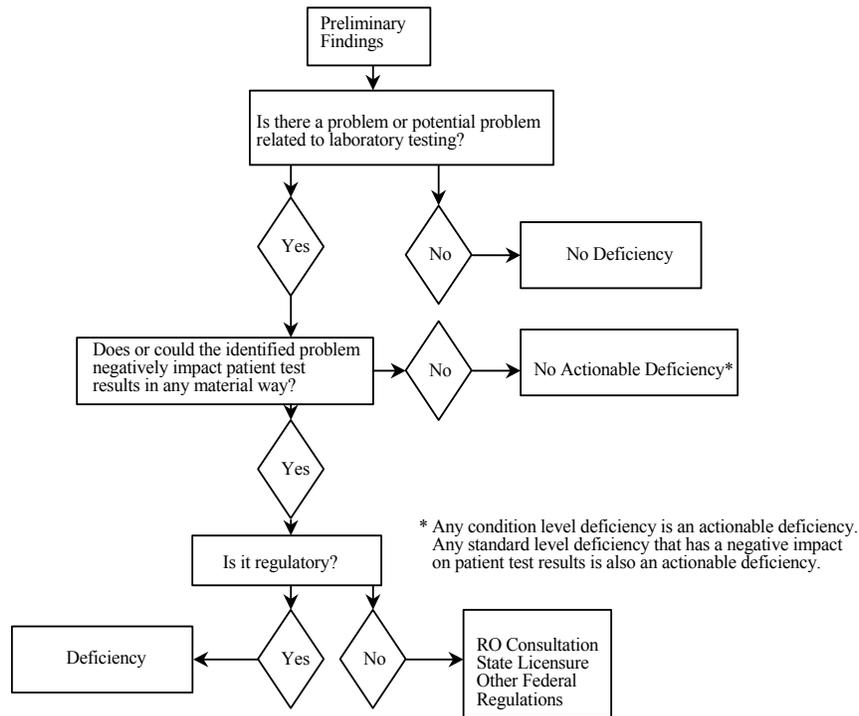
IV. ASSESSING OUTCOME OR POTENTIAL OUTCOME

If the information gathered indicates that the laboratory has established, implemented, and maintained appropriate ongoing mechanisms for ensuring quality test results by monitoring, evaluating, and resolving any problems in its practices, and your findings do not warrant a more in-depth review, conclude the survey. However, if you cannot make an assessment of the laboratory's performance based on the cross-section of information you collected, it may be necessary to expand the cross-section (e.g., number of sites, observations, or number of records). If your findings reveal potential problem areas with any test procedures, ensure the review is sufficient in breadth and depth to substantiate whether a negative or potentially negative outcome exists. If a problem or potential problem related to patient test results is found, determine the nature and seriousness of the problem.

The survey process allows the freedom to increase or decrease the number and types of records reviewed, the personnel interviewed, and the observations made as individual needs are identified.

Analyze your findings for the degree of severity, pervasiveness, survey history, frequency of occurrence, and impact on delivery of services, i.e., accuracy, reliability, and timeliness of test results. One occurrence of a deficiency directly related to a potential adverse impact on patient testing may be cited. On the other hand, some preliminary findings may have so slight an impact on outcome that they do not warrant a citation.

Refer to the following chart in assessing outcome. Refer to the next section for guidance in determining regulatory compliance.

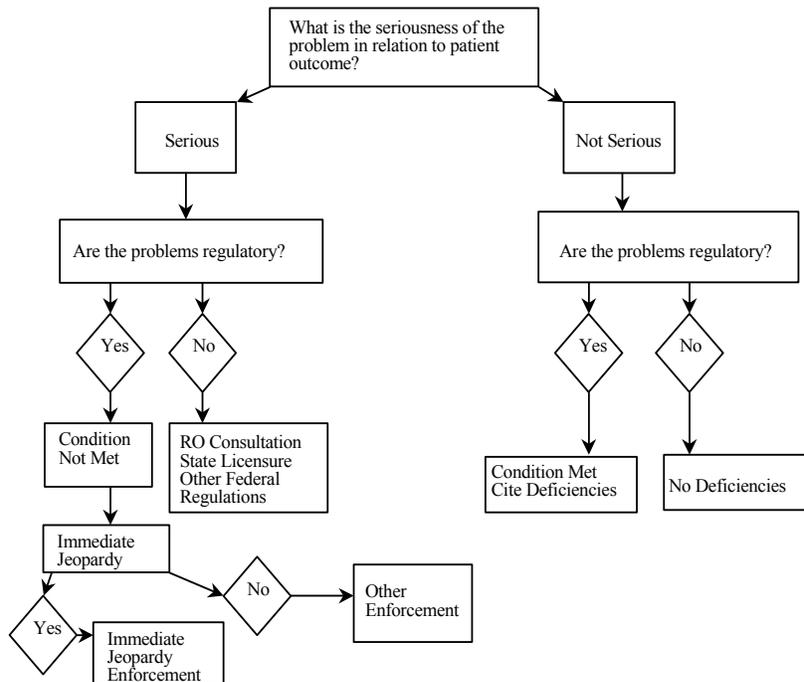


V. REGULATORY COMPLIANCE DECISION

After all necessary information has been collected and the outcome or potential outcome has been evaluated to determine if a preliminary finding constitutes a deficiency, determine if it is a condition level deficiency. Review the findings and decide if additional information and/or documentation are necessary to substantiate a deficient practice.

The number of deficiencies does not necessarily relate to whether or not a condition is found out of compliance, but rather its impact or potential impact on the quality of laboratory services and the results reported. Consider a condition out of compliance for one or more deficiencies if, in your judgment, the deficiency (ies) constitutes a significant or a serious problem that adversely affects patient test results/patient care, or has the potential for adversely affecting patient test results/patient care.

o Determining Immediate Jeopardy.--Immediate jeopardy is defined in 42 CFR §493.2 as "a situation in which immediate corrective action is necessary because the laboratory's noncompliance with one or more condition-level requirements has already caused, is causing, or is likely to cause, at any time, serious injury or harm, or death, to individuals served by the laboratory or to the health or safety of the general public. This term is synonymous with imminent and serious risk to human health and significant hazard to the public health." (See 42 CFR, section 493.1812 providing the enforcement actions to be taken when deficiencies pose immediate jeopardy.) Refer to the following chart for guidance in determining regulatory compliance.



- o What is the seriousness of the problem in relation to patient outcome?
 - Does the problem result in inaccurate test results?
 - Does the problem result in a high probability of inaccurate test results?
 - Is the situation one in which immediate corrective action is necessary because the laboratory's noncompliance has already caused or is likely to cause serious injury, harm, or death to individuals served by the laboratory or to the health or safety of the general public?
- o What are the regulatory considerations?
 - Are regulatory deficiencies identified?
 - Do the deficiencies pose an immediate jeopardy to patient health and welfare?
 - Do the deficiencies warrant removal of a certificate?
 - Is there an option for other enforcement remedies?

VI. EXIT CONFERENCE

The purpose of the exit conference is to review your findings with the laboratory and is not meant to be all-inclusive. It is the continuation of the educational survey process and the beginning of due process. The exit conference is the first opportunity for the laboratory to present additional information in response to the findings. Acknowledge staff cooperation and operational support, as appropriate, before addressing the non-compliant issues.

If immediate jeopardy or condition-level deficiencies are identified, inform the laboratory of the seriousness of the problem(s)/finding(s) and indicate that they are not final and are subject to review. Consider the following when conducting an exit conference:

- o Conduct the exit conference with the facility's administrator, director, consultant, or supervisor, and/or other invited staff;
- o Describe the requirements that are not in compliance and the findings that substantiate these deficiencies;
- o Provide the laboratory an opportunity to discuss and provide additional information regarding deficiencies. It is the laboratory's responsibility to determine the corrective action(s) necessary to remedy the problem(s);
- o Provide instructions and the time frame necessary for submitting a plan of correction as referenced in SOM Chapter 6, §6130;
- o Refer to SOM Chapter 6, §6126 for additional information on the exit conference including the presence of counsel, taping of the exit conference, and situations that would justify refusal to conduct or continue an exit conference. If a tape is made of the exit conference, get a copy before you leave;
- o Inform the facility of your intended recommendation to the RO to certify, recertify, or deny certification of the laboratory; and
- o At the exit interview, inform the laboratory (director/administrator/supervisor) of changes in test volumes which may result in fee changes.

VII. DEVELOPMENT OF THE STATEMENT OF DEFICIENCIES

Choose the most appropriate regulatory citation when documenting a deficiency. If deficient practices are a result of failure of the laboratory to properly perform quality assessment, cite the deficiency using the quality assessment requirements. If deficient practices are more basic, such as a failure of the laboratory to perform or perform correctly certain tasks or requirements, then cite the deficiency in the specific area of the regulation such as personnel, general laboratory systems, preanalytic systems, analytic systems or postanalytic systems. Supporting

information for documenting deficiencies should be complete, clear, and concise. Write deficiency statements in terms that allow a reasonably knowledgeable person to understand the aspects of the requirements that are not met. Avoid writing the same deficiency in several places. Write your statement of evidence following the format described in the Principles of Documentation.

For some cited deficiencies, The Automated Survey Processing Environment (ASPEN) system may request that you list the appropriate specialty or subspecialty identifier code(s) for each D-tag. Use the list provided on Form CMS-1557 that identifies the code number for each specialty and subspecialty (e.g., the code number for the specialty of hematology is 400). This is applicable to standard and condition-level deficiencies.

A. Standard-Level Deficiencies.--If noncompliance has been identified, cite the most specific standard available. For instance, if the deficient practice(s) is related to control procedures:

- o Cite the appropriate D-tag in the specialty/subspecialty standards under 42 CFR §§493.1261 through 1278, which are Bacteriology, Mycobacteriology, Mycology, Parasitology, Virology, Routine Chemistry, Hematology, Immunohematology, Histopathology, Cytology, Clinical Cytogenetics, and Histocompatibility if such standard is available; OR
- o Use the appropriate D-tag under 42 CFR §§493.1251 through 493.1256 and 42 CFR §§493.1281 through 493.1289, if an appropriate D-tag is NOT available in the specialty/subspecialty standards.

EXAMPLE: A laboratory performs fluid cell counts using a hemocytometer. The laboratory failed to perform manual fluid cell counts in duplicate. Use D5543.

EXAMPLE: A rheumatologist performs rheumatoid factor (RF) titers. The rheumatologist failed to include control materials for the RF titer. Use D5451.

B. Condition-Level Deficiencies.--When the deficient practice is of such a serious nature that correction is necessary for the laboratory's testing to continue, cite the most appropriate condition and document the finding using the format in the Principles of Documentation. As stated in the Principles of Documentation, the laboratory must correct those standard-level deficiencies that are used to support the condition-level noncompliance before the condition can be considered back in compliance.

Options within Subpart K:

- Specialty and Subspecialty conditions--Use these conditions when deficiencies are in a specialty or subspecialty in one or all phases of testing. D5002-D5038
- General Laboratory Systems--Use this condition when deficiencies are related only to general laboratory systems and are pervasive throughout the laboratory. D5200
- Preanalytic--Use when deficiencies are related only to the pre-analytic phase of testing and are pervasive throughout the laboratory. D5300
- Analytic--Use when deficiencies are related only the analytic phase of testing and are pervasive throughout the laboratory. D5400
- Postanalytic--Use when deficiencies are related only to the postanalytic phase of testing and are pervasive throughout the laboratory. D5800

C. Choosing the Appropriate Condition.--Review the regulatory language at each of the conditions, noting the requirements that must be met for the condition to be in compliance. For example: The condition of Bacteriology (42 CFR Part 493.1201) states the laboratory must meet the requirements at 42 CFR Part 493.1230 through 493.1256, 493.1261 and 493.1281 through 493.1299 (General Laboratory Systems, Preanalytic Systems, Analytic Systems, and Postanalytic Systems). Serious problems in one or more of these areas can cause the condition of Bacteriology to be out of compliance.

In comparison, the condition statement for Preanalytic Systems states the laboratory must meet the requirements at 42 CFR Part 493.1241, 493.1242 and 493.1249 for each specialty or subspecialty of testing. Serious preanalytic deficiencies that are pervasive throughout the laboratory (not related to specific specialties or subspecialties) could cause the condition of Preanalytic Systems to be out of compliance. Caution: An enforcement action based on non-

compliance with the condition of General Laboratory Systems, Preanalytic Systems, Analytic Systems or Postanalytic Systems would be a revocation or a suspension of the certificate and could not be a limitation of the CLIA certificate for one or more specialties.

Standard level deficiencies written in one subpart cannot be the basis for a condition in another subpart. Deficiencies in Proficiency Testing or Personnel would not be the basis for the condition of Bacteriology to be out of compliance. It is not uncommon for a surveyor to identify issues that crossover between subparts of the laboratory or the regulations, but deficiencies must be cited at the appropriate area of the regulations. For example, failures in proficiency testing may be caused by an error in specimen identification, test system malfunction, or lack of training for staff. Avoid citing more than one deficiency for the same issue, unless each deficiency focuses on a different aspect of the issue (instrument malfunction vs. staff training).

EXAMPLE:

A laboratory has deficiencies in Bacteriology under D-tags at Preanalytic Systems (D5300), Quality Control Procedures (42 CFR Part 493.1256) and the Bacteriology specialty location (42 CFR Part 493.1261). The surveyor may write the condition of Bacteriology out of compliance (D5002) based on the deficiencies cited at the three areas. If the laboratory offers testing in other specialties or subspecialties and does not make correction of the Bacteriology deficiencies, the certificate could be limited for the subspecialty of Bacteriology.

EXAMPLE:

A laboratory has deficiencies in General Laboratory Systems (D5200) that are pervasive throughout all specialties and subspecialties of testing. The surveyor would cite the condition of General Laboratory Systems out of compliance. To be in compliance with this condition, the laboratory must correct all deficiencies used to support this compliance decision. Any enforcement action would be related to the certificate and not a limitation of one or more specialties.

EXAMPLE:

A laboratory has deficiencies in Bacteriology under D-tags in the control procedures (42 CFR Part 493.1256) and at the Bacteriology specialty location (D5002), both of which are in the Analytic Systems condition and Routine Chemistry deficiencies under D-tags in control procedures (42 CFR Part 493.1256).

- The surveyor may write the condition of Bacteriology out of compliance (D5002) based on the deficiencies cited in the Bacteriology specialty area (42 CFR Part 493.1261) and the D-tags in Control Procedures area (42 CFR Part 493.1256).

- The surveyor may also write the condition of Routine Chemistry out of compliance (D5016) based on the Routine Chemistry deficiencies cited in the control procedures area (42 CFR Part 493.1256). Even though the D-tags used to determine condition-level noncompliance in Routine Chemistry are cited in the Control Procedures area, the appropriate condition to mark out of compliance is the applicable subspecialty of Routine Chemistry (D5016).

- If the laboratory performs only the subspecialties of Bacteriology and Routine Chemistry and if the deficient practices are pervasive, the surveyor may write the condition of Analytic Systems out of compliance (D5400).

In the preceding example, if the two subspecialty conditions are considered out of compliance, the laboratory can choose to correct one subspecialty without the other and the SA can recommend an adverse action to remove the subspecialty that has not been corrected. If the surveyor had cited the condition of analytic systems out of compliance, and the laboratory had only corrected one of the specialty areas, an adverse action would be taken against the entire certificate (laboratory) and not just the subspecialty. Use the conditions of General Laboratory Systems, Preanalytic Systems, Analytic Systems, and Postanalytic Systems only when the

deficiencies are pervasive throughout the laboratory and correction must be made for the entire laboratory to continue testing in any specialty.

VII. SURVEY REPORT DOCUMENTATION AND DATA ENTRY

Following each survey, as applicable, complete the following additional documentation. This information remains in the official file, either at the SA or RO. Also include Forms CMS-209, appropriate ownership information (completed by the laboratory) and the Alternative Quality Assessment Survey (AQAS) form (completed by the laboratory, if applicable) in the official file.

As applicable, complete the following:

- Form CMS-1557, Survey Report Form (CLIA);
- Form CMS-462A/B, CLIA Adverse Action Extract;
- Form CMS-2567, Statement of Deficiencies and Plan of Correction;
- Form CMS-2567B, Post Certification Revisit Report;
- Form CMS-1539, Certification and Transmittal;
- Form CMS-670, Survey Team Composition and Workload Report;
- Form CMS-282, Blood Bank Inspection Checklist and Report; and
- Form CMS-562, Medicare/Medicaid/CLIA Complaint Form.

Following the survey, enter into the CLIA/OSCAR/ODIE data system(s) any revisions, additions, or deletions to the application (Form CMS-116) information. Refer to the CLIA Systems Users Guide for specific information and instruction. Enter into the ODIE data system the Certification Kit, which consists of:

- Form CMS-1539, Certification and Transmittal;
- Form CMS-1557, Survey Report Form (CLIA) - pages 1 and 2;
- Form CMS-2567, Statement of Deficiencies and Plan of Correction; and
- Form CMS-670, Survey Team Composition and Workload Report.

Enter into the CLIA/OSCAR data system, when applicable:

- Form CMS-462A/B, CLIA Adverse Action Extract; and
- Form CMS-562, Medicare/Medicaid/CLIA Complaint Form.

The CMS Form 668B has been developed to assess the survey process from the viewpoint of the laboratory. Leave this form with all laboratories that receive either an onsite survey or the AQAS. The laboratory will complete this form.

IX. ADDITIONAL INFORMATION

A. COUNTING TESTS

Total annual volume for waived tests, if any, should be recorded on the CLIA application (Form CMS-116) in the waived testing section. The total annual volume for nonwaived tests, including PPM procedures, should be reported on the form in the Nonwaived Testing section by specialty and subspecialty. Only tests that are ordered and reported should be included in

the laboratory's test volume(s). Calculations (e.g., A/G ratio, MCH, MCHC, HCT, and T7), QC tests, and PT assays should not be counted.

- o For chemistry tests, each non-calculated analyte is counted separately (e.g., Lipid Panel consisting of a total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides equals 4 tests).

- o For complete blood counts, each measured individual analyte that is ordered and reported is counted separately. Differentials count as one test.

- o For urinalysis, microscopic and macroscopic examinations each count as one test. Macroscopics (dipsticks) are counted as one test regardless of the number of reagent pads on the strip.

- o For microbiology, susceptibility testing is counted as one test per group of antibiotics used to determine sensitivity for one organism. Cultures are counted as one per test request from each specimen regardless of the extent of identification, number of organisms isolated, and number of tests/procedures required for identification. Each gram stain or acid-fast bacteria (AFB) smear requested from the primary source is counted as one. For example, if a sputum specimen has a routine bacteriology culture and gram stain, a mycology test, and an AFB smear and culture ordered, this would be counted as five tests. For parasitology, the direct smear and the concentration and prepared slide are counted as one test.

- o For allergy testing, each allergen is counted as one test.

- o For gynecologic and nongynecologic cytology, each slide (not case) is counted as one test.

- o For immunohematology each ABO, Rh, antibody screen, cross match, or antibody identification is counted as one test.

- o For histocompatibility, each HLA typing (including disease associated antigens) is counted as one test, each HLA antibody screen is counted as one test and each HLA cross match is counted as one test. For example, a B-cell, a T-cell, and an auto-crossmatch between the same donor and recipient pair would be counted as 3 tests.

- o For histopathology, each block (not slide) is counted as one test. Autopsy services are not included. For those laboratories that perform special stains on histology slides, the test volume is determined by adding the number of special stains, including immunohistochemistry, performed on slides to the total number of specimen blocks prepared by the laboratory.

- o For cytogenetics, the number of tests is determined by the number of specimen types processed on each patient (i.e., a bone marrow and a venous blood specimen received on one patient are counted as two tests).

B. CONDUCTING SURVEYS OF MULTIPLE TESTING SITES UNDER ONE CERTIFICATE

1. As specified in 42 CFR Part 493, all not-for-profit or State or local government laboratories engaged in limited public health testing and certified under a single certificate must meet all applicable requirements of 42 CFR Part 493. Each location is subject to a survey, although not every location may be included in the cross-section of information gathered during the current certification survey period. If there is a central or primary location, include it in the initial CLIA certification survey. Select a representative portion of the remaining locations for onsite survey.

Select sites for the survey based on:

- o Types of testing performed;

- o Types of clients and/or facilities served, e.g., pediatric, geriatric, residential/emergency care, or health assessment screens;
- o Location(s) participating in PT; and
- o Problems or complaints identified either at the central or primary location, or other testing sites.

2. In a hospital, laboratory testing sites under one certificate should be inspected using the criteria listed above.

3. Temporary testing sites, including mobile units, should be inspected using the criteria listed in A above. Refer to the SOM Chapter 6, §6034 to assist with determining what constitutes a mobile unit. Every effort should be made to schedule the survey to coincide with testing at temporary locations.

Many Home Health Agencies (HHAs) may have fallen under the exception contained in the CLIA regulations for not-for-profit or government entities involved in limited public health testing. HHAs may also fall under the CLIA certification exception for laboratories with temporary testing locations. Refer to Transmittal Number 98-1 (Program Memorandum, State Survey Agencies) to assist with determining (on a case-by-case basis) whether or not a Medicare HHA actually qualifies to have multiple testing sites under a single CLIA certificate.

A laboratory having multiple sites under one certificate is required to enroll in only one PT program(s) for each specialty/subspecialty/analyte tested under that certificate even though the same analyte may be tested at multiple locations using different test systems, methodologies, or personnel.

Assure that PT records indicate the location at which the tests were performed, and that all other locations have been compared with the system selected for PT, as specified in 42 CFR 493.1281(a).

A condition may be considered out of compliance for deficiencies found at one or more locations.

C. CONDUCTING SURVEYS OF WAIVED TESTS

In any laboratory holding a CLIA certificate, waived tests are not subject to routine survey. A survey of waived tests may be conducted only when authorized by the RO to:

- o Collect information on waived tests;
- o Determine if a laboratory is testing outside their certificate;
- o Investigate an alleged complaint; and/or
- o Determine if the performance of such tests poses a situation of immediate jeopardy.

D. CONDUCTING SURVEYS OF CERTIFICATE FOR PPM PROCEDURES

If a laboratory holds a Certificate for PPM procedures, do not conduct a certification or recertification survey of these facilities. However, a survey may be conducted as specified in 42 CFR Part 493, Subpart Q (i.e., randomly to determine whether the laboratory is performing tests in addition to those listed as PPM procedures or waived tests, to collect information regarding the appropriateness of tests specified as PPM, to determine that testing is being performed or the laboratory is being operated in a manner that does not constitute an imminent and serious risk to the public, and to evaluate a complaint from the public). When performing a survey of PPM procedures, the appropriate requirements in 42 CFR Part 493 Subparts H, J, K, M and Q apply.

Appendix C
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Services
(Rev. 32 , 02-13-2004)

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D-Tag numbers immediately precede the description of regulation.

Subpart A--General Provisions

§493.1 Basis and Scope.

This part sets forth the conditions that all laboratories must meet to be certified to perform testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). It implements sections 1861(e) and (j), the sentence following section 1861(s)(13), and 1902(a)(9) of the Social Security Act, and section 353 of the Public Health Service Act. This part applies to all laboratories as defined under "laboratory" in §493.2 of this part. This part also applies to laboratories seeking payment under the Medicare and Medicaid programs. The requirements are the same for Medicare approval as for CLIA certification.

§493.2 Definitions.

As used in this part, unless the context indicates otherwise--

Accredited institution means a school or program which--

- (a) Admits as regular student only persons having a certificate of graduation from a school providing secondary education, or the recognized equivalent of such certificate;
- (b) Is legally authorized within the State to provide a program of education beyond secondary education;
- (c) Provides an educational program for which it awards a bachelor's degree or provides not less than a 2-year program which is acceptable toward such a degree, or provides an educational program for which it awards a master's or doctoral degree;
- (d) Is accredited by a nationally recognized accrediting agency or association.

This definition includes any foreign institution of higher education that HHS or its designee determines meets substantially equivalent requirements.

Interpretive Guidelines §493.2(d)

HHS has determined that Foreign academic credential evaluation may be performed by any nationally recognized organization. Equivalency evaluations may be performed by these organizations and their affiliates. Such organizations may include the National Association Credential Evaluation Services, Inc. (NACES) (<http://www.naces.org>) and the Association of International Credential Evaluators, Inc. (AICE) (<http://www.aice-eval.org>) or telephone (310) 550-3305.. The Internet may also be searched for other such nationally recognized organizations and affiliates.

A nationally recognized accrediting agency or association, recognized by the Secretary means a school or program that is approved by:

- *The Council of Medical Education of the American Medical Association (AMA). AMA schools are listed in the Allied Medical Education Directory and may be obtained from the AMA Order Department at 515 North Dearborn Chicago, Illinois 60610;*
- *One of the eight Regional accreditation programs [commission] listed in the latest edition of Education Directory that can be obtained from the U.S. Department of Education at <http://www.ed.gov> or by telephone at 1-800-872-5327;*
- *New York Board of Regents (<http://www.nysed.gov>) or by telephone at (518) 474-5844;*
- *National Institutional and Specialized Accrediting Bodies includes the Accrediting Bureau of Health Education schools. The web address is: www.abhes.gov or by telephone at (703) 917-9503.*

Individuals qualify by obtaining the appropriate degree after completing the academic requirements and training in an accredited school at a time when the school is

accredited. If there is any question about the accreditation status of the school, contact the accrediting agency involved.

If there is an issue concerning the confirming of a particular degree by an institution, contact the school involved for a decision.

States have varying degrees of control over education. However, there are several associations of regional or national scope that provide assistance pertinent to identifying accredited institutions and educational programs.

Personnel that perform tests of moderate and/or high complexity in a CLIA certified laboratory must meet specific education, training, and experience requirements. Individuals who attended foreign schools must have an evaluation of their credentials determining equivalency of their education to education obtained in the United States (US). The equivalency evaluations may be performed by a nationally recognized organization.

Accredited laboratory means a laboratory that has voluntarily applied for and been accredited by a private, nonprofit accreditation organization approved by CMS in accordance with this part;

Adverse action means the imposition of a principal or alternative sanction by CMS.

ALJ stands for Administrative Law Judge.

Alternative sanctions means sanctions that may be imposed in lieu of or in addition to principal sanctions. The term is synonymous with “intermediate sanctions” as used in section 1846 of the Act.

Analyte means a substance or constituent for which the laboratory conducts testing.

Approved accreditation organization for laboratories means a private, nonprofit accreditation organization that has formally applied for and received CMS’s approval based on the organization’s compliance with this part.

Approved State laboratory program means a licensure or other regulatory program for laboratories in a State, the requirements of which are imposed under State law, and the State laboratory program has received CMS approval based on the State’s compliance with this part.

Authorized person means an individual authorized under State law to order tests or receive test results, or both.

Calibration means a process of testing and adjusting an instrument or test system to establish a correlation between the measurement response and the concentration or amount of the substance that is being measured by the test procedure.

Calibration verification means the assaying of materials of known concentration in the same manner as patient specimens to substantiate the instrument or test system’s calibration throughout the reportable range for patient test results.

Challenge means, for quantitative tests, an assessment of the amount of substance or analyte present or measured in a sample. For qualitative tests, a challenge means the determination of the presence or the absence of an analyte, organism, or substance in a sample.

CLIA means the Clinical Laboratory Improvement Amendments of 1988.

CLIA certificate means any of the following types of certificates issued by CMS or its agent:

(1) Certificate of compliance means a certificate issued to a laboratory after an inspection that finds the laboratory to be in compliance with all applicable condition level requirements, or reissued before the expiration date, pending an appeal, in accordance with §493.49, when an inspection has found the laboratory to be out of compliance with one or more condition level requirements.

(2) Certificate for provider-performed microscopy (PPM) procedures means a certificate issued or reissued before the expiration date, pending an appeal, in accordance with §493.47, to a laboratory in which a physician, midlevel practitioner or dentist performs no tests other than PPM procedures and, if desired, waived tests listed in §493.15(c).

(3) Certificate of accreditation means a certificate issued on the basis of the laboratory’s accreditation by an accreditation organization approved by CMS (indicating that the laboratory is

deemed to meet applicable CLIA requirements) or reissued before the expiration date, pending an appeal, in accordance with §493.61, when a validation or complaint survey has found the laboratory to be noncompliant with one or more CLIA conditions.

(4) Certificate of registration or registration certificate means a certificate issued or reissued before the expiration date, pending an appeal, in accordance with §493.45, that enables the entity to conduct moderate or high complexity laboratory testing or both until the entity is determined to be in compliance through a survey by CMS or its agent; or in accordance with §493.57 to an entity that is accredited by an approved accreditation organization.

(5) Certificate of waiver means a certificate issued or reissued before the expiration date, pending an appeal, in accordance with §493.37, to a laboratory to perform only the waived tests listed at §493.15(c).

CLIA-exempt laboratory means a laboratory that has been licensed or approved by a State where CMS has determined that the State has enacted laws relating to laboratory requirements that are equal to or more stringent than CLIA requirements and the State licensure program has been approved by CMS in accordance with subpart E of this part.

CMS agent means an entity with which CMS arranges to inspect laboratories and assess laboratory activities against CLIA requirements and may be a State survey agency, a private, nonprofit organization other than an approved accreditation organization, a component of HHS, or any other governmental component CMS approves for this purpose. In those instances where all of the laboratories in a State are exempt from CLIA requirements, based on the approval of a State's exemption request, the State survey agency is not the CMS agent.

Condition level deficiency means noncompliance with one or more condition level requirements.

Condition level requirements means any of the requirements identified as "conditions" in subparts G through Q of this part.

Credible allegations of compliance means a statement or documentation that--

- (1) Is made by a representative of a laboratory that has a history of having maintained a commitment to compliance and of taking corrective action when required;
- (2) Is realistic in terms of its being possible to accomplish the required corrective action between the date of the exit conference and the date of the allegation; and
- (3) Indicates that the problem has been resolved.

Dentist means a doctor of dental medicine or doctor of dental surgery licensed by the State to practice dentistry within the State in which the laboratory is located.

Equivalency means that an accreditation organization's or a State laboratory program's requirements, taken as a whole, are equal to or more stringent than the CLIA requirements established by CMS, taken as whole. It is acceptable for an accreditation organization's or State laboratory program's requirements to be organized differently or otherwise vary from the CLIA requirements, as long as (1) all of the requirements taken as a whole would provide at least the same protection as the CLIA requirements taken as a whole; and (2) a finding of noncompliance with respect to CLIA requirements taken as a whole would be matched by a finding of noncompliance with the accreditation or State requirements taken as a whole.

FDA-cleared or approved test system means a test system cleared or approved by the FDA through the premarket notification (510(k)) or premarket approval (PMA) process for in-vitro diagnostic use. Unless otherwise stated, this includes test systems exempt from FDA premarket clearance or approval.

HHS means the Department of Health and Human Services, or its designee.

Immediate jeopardy means a situation in which immediate corrective action is necessary because the laboratory's noncompliance with one or more condition level requirements has already caused, is causing, or is likely to cause, at any time, serious injury or harm, or death, to individuals served by the laboratory or to the health or safety of the general public. This term is synonymous with imminent and serious risk to human health and significant hazard to the public health.

Intentional violation means knowing and willful noncompliance with any CLIA condition.

Kit means all components of a test that are packaged together.

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

Interpretive Guideline

Currently, in-vivo and externally attached patient dedicated monitoring devices, e.g., as pulse oximetry, SvO2 pulmonary artery catheters, capnographs, are not subject to CLIA. Should it be determined at a later date that they are subject to CLIA, proper notice and opportunity for public comment will be provided.

Tissue embedding, sectioning, and staining in Pathology are considered part of specimen preparation, not a laboratory test, and do not fall under CLIA. Macroscopic (gross) examinations of specimens must be performed by an individual qualified under §493.1449(l)(1). However, the laboratory that interprets histopathology preparations must ensure that a control slide is included with each slide or group of slides for differential or special stains as required under §4993.1273. Also, laboratories that screen or interpret cytopathology slides are responsible for ensuring that cytology slides are stained in compliance with the applicable requirements at §493.1274(b). In addition for laboratories that prepare cytology specimens using automated or semi-automated liquid-based preparatory techniques, they must comply with the manufacturer's instructions for the preanalytic, analytic, and postanalytic phases of testing.

Midlevel practitioner means a nurse midwife, nurse practitioner, or physician assistant, licensed by the State within which the individual practices, if such licensing is required in the State in which the laboratory is located.

Nonwaived test means any test system, assay, or examination that has not been found to meet the statutory criteria specified at section 353(d)(3) of the Public Health Service Act.

Operator means the individual or group of individuals who oversee all facets of the operation of a laboratory and who bear primary responsibility for the safety and reliability of the results of all specimen testing performed in that laboratory. The term includes –

- (1) A director of the laboratory if he or she meets the stated criteria; and
- (2) The members of the board of directors and the officers of a laboratory that is a small corporation under subchapter S of the Internal Revenue Code.

Owner means any person who owns any interest in a laboratory except for an interest in a laboratory whose stock and/or securities are publicly traded. (That is e.g., the purchase of shares of stock or securities on the New York Stock Exchange in a corporation owning a laboratory would not make a person an owner for the purpose of this regulation.)

Party means a laboratory affected by any of the enforcement procedures set forth in this subpart, by CMS or the OIG, as appropriate.

Performance characteristic means a property of a test that is used to describe its quality, e.g., accuracy, precision, analytical sensitivity, analytical specificity, reportable range, reference range, etc.

Performance specification means a value or range of values for a performance characteristic, established or verified by the laboratory, that is used to describe the quality of patient test results.

Physician means an individual with a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine degree who is licensed by the State to practice medicine, osteopathy, or podiatry within the State in which the laboratory is located.

Principal sanction means the suspension, limitation, or revocation of any type of CLIA certificate or the cancellation of the laboratory's approval to receive Medicare payment for its services.

Prospective laboratory means a laboratory that is operating under a registration certificate or is seeking any of the three other types of CLIA certificates.

Rate of disparity means the percentage of sample validation inspections for a specific accreditation organization or State where CMS, the State survey agency or other CMS agent finds noncompliance with one or more condition level requirements but no comparable deficiencies were cited by the accreditation organization or the State, and it is reasonable to conclude that the deficiencies were present at the time of the most recent accreditation organization or State licensure inspection.

Example: Assume the State survey agency, CMS or other CMS agent performs 200 sample validation inspections for laboratories accredited by a single accreditation organization or licensed in an exempt State during a validation review period and finds that 60 of the 200 laboratories had one or more condition level requirements out of compliance. CMS reviews the validation and accreditation organization's or State's inspections of the validated laboratories and determines that the State or accreditation organization found comparable deficiencies in 22 of the 60 laboratories and it is reasonable to conclude that deficiencies were present in the remaining 38 laboratories at the time of the accreditation organization's or State's inspection. Thirty-eight divided by 200 equals a 19 percent rate of disparity.

Referee laboratory means a laboratory currently in compliance with applicable CLIA requirements, that has had a record of satisfactory proficiency testing performance for all testing events for at least one year for a specific test, analyte, subspecialty, or specialty and has been designated by an HHS approved proficiency testing program as a referee laboratory for analyzing proficiency testing specimens for the purpose of determining the correct response for the specimens in a testing event for that specific test, analyte, subspecialty, or specialty.

Reference range means the range of test values expected for a designated population of individuals, e.g., 95 percent of individuals that are presumed to be healthy (or normal).

Reportable range means the span of test result values over which the laboratory can establish or verify the accuracy of the instrument or test system measurement response.

Sample in proficiency testing means the material contained in a vial, on a slide, or other unit that contains material to be tested by proficiency testing program participants. When possible, samples are of human origin.

State includes, for purposes of this part, each of the 50 States, the District of Columbia, the Commonwealth of Puerto Rico, the Virgin Islands and a political subdivision of a State where the State, acting pursuant to State law, has expressly delegated powers to the political subdivision sufficient to authorize the political subdivision to act for the State in enforcing requirements equal to or more stringent than CLIA requirements.

State licensure means the issuance of a license to, or the approval of, a laboratory by a State laboratory program as meeting standards for licensing or approval established under State law.

State licensure program means a State laboratory licensure or approval program.

State survey agency means the State health agency or other appropriate State or local agency that has an agreement under section 1864 of the Social Security Act and is used by CMS to perform surveys and inspections.

Substantial allegation of noncompliance means a complaint from any of a variety of sources (including complaints submitted in person, by telephone, through written correspondence, or in newspaper or magazine articles) that, if substantiated, would have an impact on the health and safety of the general public or of individuals served by a laboratory and raises doubts as to a laboratory's compliance with any condition level requirement.

Target value for quantitative tests means either the mean of all participant responses after removal of outliers (those responses greater than 3 standard deviations from the original mean) or the mean established by definitive or reference methods acceptable for use in the National Reference System for the Clinical Laboratory (NRSCL) by NCCLS. In instances where definitive or reference methods are not available or a specific method's results demonstrate bias that is not observed with actual patient specimens, as determined by a defensible scientific protocol, a comparative method or a method group ("peer" group) may be used. If the method group is less than 10 participants, "target value" means the overall mean after outlier removal (as defined above) unless acceptable scientific reasons are available to indicate that such an evaluation is not appropriate.

Test system means the instructions and all of the instrumentation, equipment, reagent, and supplies needed to perform an assay or examination and generate test results.

Unsatisfactory proficiency testing performance means failure to attain the minimum satisfactory score for an analyte, test, subspecialty, or specialty for a testing event.

Unsuccessful participation in proficiency testing means any of the following:

(1) Unsatisfactory performance for the same analyte in two consecutive or two out of three testing events.

(2) Repeated unsatisfactory overall testing event scores for two consecutive or two out of three testing events for the same specialty or subspecialty.

(3) An unsatisfactory testing event score for those subspecialties not graded by analyte (that is, bacteriology, mycobacteriology, virology, parasitology, mycology, blood compatibility, immunohematology, or syphilis serology) for the same subspecialty for two consecutive or two out of three testing events.

(4) Failure of a laboratory performing gynecologic cytology to meet the standard at §493.855.

Unsuccessful proficiency testing performance means a failure to attain the minimum satisfactory score for an analyte, test, subspecialty, or specialty for two consecutive or two of three consecutive testing events.

Validation review period means the one year time period during which CMS conducts validation inspections and evaluates the results of the most recent surveys performed by an accreditation organization or State laboratory program.

Waived test means a test system, assay, or examination that HHS has determined meets the CLIA statutory criteria as specified for waiver under section 353(d)(3) of the Public Health Service Act.

§493.3 Applicability.

(a) **Basic rule.** Except as specified in paragraph (b) of this section, a laboratory will be cited as out of compliance with section 353 of the Public Health Service Act unless it--

(1) Has a current, unrevoked or unsuspended certificate of waiver, a registration certificate, certificate of compliance, certificate for PPM procedures, or certificate of accreditation issued by HHS applicable to the category of examinations or procedures performed by the laboratory; or

(2) Is CLIA-exempt.

(b) **Exception.** These rules do not apply to components or functions of--

(1) Any facility or component of a facility that only performs testing for forensic purposes;

(2) Research laboratories that test human specimens but do not report patient specific results for the diagnosis, prevention or treatment of any disease or impairment of, or the assessment of the health of individual patients; or

(3) Laboratories certified by the Substance Abuse and Mental Health Service Administration (SAMSHA), in which drug testing is performed which meets SAMSHA guidelines and regulations. However, all other testing conducted by a SAMSA-certified laboratory is subject to this rule.

Interpretive Guidelines §493.3(b)

The purpose for which the test is conducted, not the test itself, determines whether a facility conducting testing is subject to the CLIA requirements. Testing that is used to gather evidence for legal purposes, and is not performed for purposes of clinical treatment, medical diagnosis, health assessment or disease prevention is not subject to CLIA.

For blood donor screening, the FDA requirements are product-related, while CLIA requirements are donor/recipient-related. Tests such as hepatitis, HIV and syphilis serology, among others, are used in donor screening to assess the health of the person donating blood, one of the activities that come within the statutory definition of "laboratory". Therefore, the performance of these tests must meet CLIA requirements.

Industrial laboratories that monitor employee health, insurance company laboratories that assess an individual's health for insurance purposes, health maintenance organizations, and other facilities such as pharmacies and health fairs that perform screening test procedures are also subject to CLIA requirements.

Individuals who self-administer a test in their own home with a device that has been cleared specifically for home use by the FDA are not regulated under CLIA. To the extent that a home health agency (HHA) or hospice that is providing care in an individual's home is engaged solely in assisting an individual in performing a test, by virtue of that activity, CLIA requirements for the HHA or hospice do not apply. However, an HHA or hospice that performs laboratory testing on individuals that meets the definition for laboratory testing in §493.2 is subject to CLIA requirements.

(c) Federal laboratories. Laboratories under the jurisdiction of an agency of the Federal Government are subject to the rules of this part, except that the Secretary may modify the application of such requirements as appropriate.

Interpretive Guidelines §493.3(c)

Refer to §§6002 and 6022 of the State Operations Manual (SOM) to assist in distinguishing which laboratories are under the jurisdiction of the Federal government for purposes of inspecting for CLIA.

§493.5 Categories of tests by complexity.

(a) Laboratory tests are categorized as one of the following:

(1) Waived tests.

(2) Tests of moderate complexity, including the subcategory of PPM procedures.

(3) Tests of high complexity.

(b) A laboratory may perform only waived test, only test of moderate complexity, only PPM procedures, only tests of high complexity or any combination of these tests.

(c) Each laboratory must be either CLIA-exempt or possess one of the following CLIA certificates, as defined in §493.2:

(1) Certificate of registration or registration certificate.

(2) Certificate of waiver.

(3) Certificate for PPM procedures.

(4) Certificate of compliance.

(5) Certificate of accreditation.

§493.15 Laboratories performing waived tests.

(a) Requirement. Tests for certificate of waiver must meet the descriptive criteria specified in paragraph (b) of this section.

(b) Criteria. Test systems are simple laboratory examinations and procedures which--

(1) Are cleared by FDA for home use;

(2) Employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible; or

(3) Pose no reasonable risk of harm to the patient if the test is performed incorrectly.

D1000

(c) Certificate of waiver tests. A laboratory may qualify for a certificate of waiver under section 353 of the PHS Act if it restricts the tests that it performs to one or more of the

following tests or examinations (or additional tests added to this list as provided under paragraph (d) of this section) and no others:

Interpretive Guidelines §493.15(c)

Cite D1000 on the CMS-2567 and solicit a Plan of Correction when a laboratory has failed to obtain a registration certificate before performing and reporting patient results for tests not categorized as waived. To determine which tests are categorized as waived or nonwaived (i.e., moderate or high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/cli/index.html]. Test systems, assays, and examinations not yet classified are considered high complexity. Significant deficiencies cited under this condition may also indicate deficiencies under personnel responsibilities.

Notify the RO of a possible action by the OIG if the laboratory does not obtain the appropriate certificate or cease non-waived testing.

(1) Dipstick or Tablet Reagent Urinalysis (non-automated) for the following:

- (i) Bilirubin;**
- (ii) Glucose;**
- (iii) Hemoglobin;**
- (iv) Ketone;**
- (v) Leukocytes;**
- (vi) Nitrite;**
- (vii) pH;**
- (viii) Protein;**
- (ix) Specific gravity; and**
- (x) Urobilinogen.**

(2) Fecal occult blood;

(3) Ovulation tests--visual color comparison tests for human luteinizing hormone;

(4) Urine pregnancy tests - visual color comparison tests;

(5) Erythrocyte sedimentation rate -non-automated;

(6) Hemoglobin - copper sulfate - non-automated;

(7) Blood glucose by glucose monitoring devices cleared by the FDA specifically for home use;

(8) Spun microhematocrit; and

(9) Hemoglobin by single analyte instruments with self-contained or component features to perform specimen/reagent interaction, providing direct measurement and readout.

(d) Revisions to criteria for test categorization and the list of waived tests.

HHS will determine whether a laboratory test meets the criteria listed under paragraph (b) of this section for a waived test. Revisions to the list of waived tests approved by HHS will be published in the FEDERAL REGISTER in a notice with opportunity for comment.

D1001

(e) Laboratories eligible for a certificate of waiver must--

(1) Follow manufacturers' instructions for performing the test; and

(2) Meet the requirements in Subpart B, Certificate of Waiver, of this part.

Interpretive Guidelines §493.15(e)

Tests listed on the waiver list in §493.15(c) are not subject to routine survey. A survey of waived tests may be conducted only when authorized by the RO in the following instances:

- o To collect information regarding the appropriateness of waived tests;*
- o If a complaint is alleged; or*
- o You have information that the performance of such tests poses a situation of immediate jeopardy; and*

- o To determine if a laboratory is performing only tests categorized as waived. Refer to §§493.1773 and 493.1775 for additional guidelines for inspecting laboratories issued a certificate of waiver.
-

§493.17 Test Categorization.

(a) ***Categorization by criteria.*** Notices will be published in the FEDERAL REGISTER which list each specific test system, assay, and examination categorized by complexity. Using the seven criteria specified in this paragraph for categorizing tests of moderate or high complexity, each specific laboratory test system, assay, and examination will be graded for level of complexity by assigning scores of 1, 2, or 3 within each criteria. The score of “1” indicates the lowest level of complexity, and the score of “3” indicates the highest level. These scores will be totaled. Test systems, assays or examination receiving scores of 12 or less will be categorized as moderate complexity, while those receiving scores above 12 will be categorized as high complexity.

NOTE: A score of “2” will be assigned to a criteria heading when the characteristics for a particular test are intermediate between the description listed for scores of “1” and “3.”

(1) Knowledge.

(i) **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.

(ii) **Score 3.** (A) Specialized scientific and technical knowledge is essential to perform preanalytic, analytic or postanalytic phases of the testing.

(2) Training and experience.

(i) **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.

(ii) **Score 3.** (A) Specialized training is essential to perform the preanalytic, analytic or postanalytic testing process; or (B) Substantial experience may be necessary for analytic test performance.

(3) Reagents and materials preparation.

(i) **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.

(ii) **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.

(i) **Score 1.** Operational steps are either automatically executed (such as pipetting, temperature monitoring, or timing of steps), or are easily controlled.

(ii) **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.

(i) **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.

(ii) **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.

(i) **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.

(ii) **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.

(i) **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; and

(ii) **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.

(b) Revisions to the criteria for categorization.

The Clinical Laboratory Improvement Advisory Committee, as defined in subpart T of this part, will conduct reviews upon request of HHS and recommend to HHS revisions to the criteria for categorization of tests.

(c) Process for device/test categorization utilizing the scoring system under §493.17(a).

(1)(i) For new commercial test systems, assays, or examinations, the manufacturer, as part of its 510(k) and PMA application to FDA, will submit supporting data for device/test categorization. FDA will determine the complexity category, notify the manufacturers directly, and will simultaneously inform both CMS and CDC of the device/test category. FDA will consult with CDC concerning test categorization in the following three situations:

(A) When categorizing previously uncategorized new technology;

(B) When FDA determines it to be necessary in cases involving a request for a change in categorization; and

(C) If a manufacturer requests review of a categorization decision by FDA in accordance with 21 CFR 10.75.

(ii) Test categorization will be effective as of the notification to the applicant.

(2) For test systems, assays, or examinations not commercially available, a laboratory or professional group may submit a written request for categorization to PHS. These requests will be forwarded to CDC for evaluation; CDC will determine complexity category and notify the applicant, CMS, and FDA of the categorization decision. In the case of request for a change of category or for previously uncategorized new technology, PHS will receive the request application and forward it to CDC for categorization.

(3) A request for recategorization will be accepted for review if it is based on new information not previously submitted in a request for categorization or recategorization by the same applicant and will not be considered more frequently than once per year.

(4) If a laboratory test system, assay or examination does not appear on the lists of tests in the FEDERAL REGISTER notices, it is considered to be a test of high complexity until PHS, upon request, reviews the matter and notifies the applicant of its decision. Test categorization is effective as of the notification to the applicant.

(5) PHS will publish revisions periodically to the list of moderate and high complexity tests in the FEDERAL REGISTER in a notice with opportunity for comment.

Interpretive Guidelines §493.17

To determine which tests are categorized as waived or nonwaived (i.e., moderate or high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/clia/index.html]. Test systems, assays, and examinations not yet classified are considered high complexity.

Significant deficiencies cited under this condition may also indicate deficiencies under personnel responsibilities.

§493.19 Provider-performed microscopy (PPM) procedures.

- (a) **Requirement.** To be categorized as a PPM procedure, the procedure must meet the criteria specified in paragraph (b) of this section.
- (b) **Criteria.** Procedures must meet the following specifications:
- (1) The examination must be personally performed by one of the following practitioners:
 - (i) A physician during the patient's visit on a specimen obtained from his or her own patient or from a patient of a group medical practice of which the physician is a member or an employee.
 - (ii) A midlevel practitioner, under the supervision of a physician or in independent practice only if authorized by the State, during the patient's visit on a specimen obtained from his or her own patient or from a patient of a clinic, group medical practice, or other health care provider of which the midlevel practitioner is a member or an employee.
 - (iii) A dentist during the patient's visit on a specimen obtained from his or her own patient or from a patient of a group dental practice of which the dentist is a member or an employee.
 - (2) The procedure must be categorized as moderately complex.
 - (3) The primary instrument for performing the test is the microscope, limited to bright-field or phase-contrast microscopy.
 - (4) The specimen is labile or delay in performing the test could compromise the accuracy of the test result.
 - (5) Control materials are not available to monitor the entire testing process.
 - (6) Limited specimen handling or processing is required.
- (c) **Provider-performed microscopy (PPM) examinations.** A laboratory may qualify to perform tests under this section if it restricts PPM examinations to one or more of the following procedures (or additional procedures added to this list as provided under paragraph (d) of this section), waived tests and no others:
- (1) All direct wet mount preparations for the presence or absence of bacteria, fungi, parasites, and human cellular elements.
 - (2) All potassium hydroxide (KOH) preparations.
 - (3) Pinworm examinations.
 - (4) Fern tests.
 - (5) Post-coital direct, qualitative examinations of vaginal or cervical mucous.
 - (6) Urine sediment examinations.
 - (7) Nasal smears for granulocytes.
 - (8) Fecal leukocyte examinations.
 - (9) Qualitative semen analysis (limited to the presence or absence of sperm and detection of motility).
- (d) **Revision to criteria and the list of PPM procedures.**
- (1) The CLIAC conducts reviews upon HHS' request and recommends to HHS revisions to the criteria for categorization of procedures.
 - (2) HHS determines whether a laboratory procedure meets the criteria listed under paragraph (b) of this section for a PPM procedure. Revisions to the list of PPM procedures proposed by HHS are published in the FEDERAL REGISTER as a notice with an opportunity for public comment.
- (e) **Laboratory requirements.** Laboratories eligible to perform PPM examinations must--
- (1) Meet the applicable requirements in subpart C or subpart D, and subparts F, H, J, K, and M of this part.
 - (2) Be subject to inspection as specified under subpart Q of this part.

§493.20 Laboratories performing tests of moderate complexity.

Interpretive Guidelines §493.20

See §6030 of the SOM for instructions on handling a laboratory operating without a CLIA certificate.

(a) A laboratory may qualify for a certificate to perform tests of moderate complexity provided that it restricts its test performance to waived tests or examinations and one or more tests or examinations meeting criteria for tests of moderate complexity including the subcategory of PPM procedures.

(b) A laboratory that performs tests or examinations of moderate complexity must meet the applicable requirements in subpart C or subpart D, and subparts F, H, J, K, M, and Q of this part. Under a registration certificate or certificate of compliance, laboratories also performing PPM procedures must meet the inspection requirements at §§ 493.1773 and 493.1777.

(c) If the laboratory also performs waived tests, compliance with subparts H, J, K, and M of this part is not applicable to the waived tests. However, the laboratory must comply with the requirements in §§493.15(e), 493.1773, and 493.1775.

§493.25 Laboratories performing tests of high complexity.

Interpretive Guidelines §493.25

See §6030 of the SOM for instructions on handling a laboratory operating without a CLIA certificate.

(a) 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(a).

(b) A laboratory performing one or more tests of high complexity must meet the applicable requirements of subparts C or subpart D, and subparts F, H, J, K, M, and Q of this part.

(c) If the laboratory also performs tests of moderate complexity, the applicable requirements of subparts H, J, K, M, and Q of this part must be met. Under a registration certificate or certificate of compliance, PPM procedures must meet the inspection requirements in §§493.1773 and 493.1777.

(d) If the laboratory also performs waived tests, the requirements of subparts H, J, K, and M are not applicable to the waived tests. However, the laboratory must comply with the requirements in §§493.15(e), 493.1773 and 493.1775.

Subpart B--Certificate of Waiver

§493.35 Application for a certificate of waiver

(a) *Filing of application.* Except as specified in paragraph (b) of this section, a laboratory performing only one or more waived tests listed in §435.15(b) of this chapter must file a separate application for each laboratory location.

(b) *Exceptions.* (1) Laboratories that are not at a fixed location, that is, laboratories that move from testing site to testing site, such as mobile units providing laboratory testing, health screening fairs, or other temporary testing locations may be covered under the certificate of the designated primary site or home base, using its address.

Interpretive Guidelines §493.35(b)(1)

A mobile unit is a laboratory located within a self-contained vehicle, such as a van. The vehicle moves from location to location to perform laboratory testing activities. All pre-analytic, analytic and post analytic activities are conducted within the confines of the vehicle.

Laboratories with multiple testing sites or mobile laboratories eligible for a single certificate should obtain a separate certificate for each State in which testing is performed.

If a mobile laboratory operates in more than one State and does not obtain a separate certificate from each State, contact the RO to determine which State conducts the inspection.

Each laboratory that moves from testing site to testing site, or has a temporary testing location, should provide the survey agency with the home base or central dispatch phone number so that an updated schedule of the location of testing and the hours of operation can be obtained upon request.

Mobile vans will be distinguished by the vehicle identification number (VIN #). See §6034 of the SOM for additional information on mobile laboratories.

(2) Not-for-profit or Federal, State, or local government laboratories that engage in limited (not more than a combination of 15 moderately complex or waived tests per certificate) public health testing may file a single application.

Interpretive Guidelines §493.35(b)(2)

See §6008 of the SOM for the definition for limited public health testing.

See §6008 of the SOM for assistance in determining whether laboratories under the same ownership can file a single application.

(3) Laboratories within a hospital that are located at contiguous buildings on the same campus and under common direction may file a single application or multiple applications for the laboratory sites within the same physical location or street address.

Interpretive Guidelines §493.35(b)(3)

"Common direction" means that all testing sites are under one designated director.

"Street address" is the address assigned by the Post Office and is the physical location of the laboratory. The street address may be different from the mailing address, which can be a Post Office box or a billing address. For large hospitals, such as a university campus facility, that may contain laboratories in separate buildings, consult with the RO to determine if the hospital is eligible for a single certificate.

(c) Application format and contents. The application must--

(1) Be made to HHS or its designee on a form or forms prescribed by HHS;

(2) Be signed by an owner, or by an authorized representative of the laboratory who attests that the laboratory will be operated in accordance with requirements established by the Secretary under section 353 of the PHS Act; and

(3) Describe the characteristics of the laboratory operation and the examinations and other test procedures performed by the laboratory including--

(i) The name and the total number of test procedures and examinations performed annually (excluding tests the laboratory may run for quality control, quality assessment or proficiency testing purposes;

(ii) The methodologies for each laboratory test procedure or examination performed, or both; and

(iii) The qualifications (educational background, training, and experience) of the personnel directing and supervising the laboratory and performing the laboratory examinations and test procedures.

(d) Access requirements. Laboratories that perform one or more waived tests listed in §493.15(c) and no other tests must meet the following conditions:

Interpretive Guidelines §493.35(d)

Cite deficiencies for not following manufacturer's instructions at §493.15(e). (D1001)

(1) Make records available and submit reports to HHS as HHS may reasonably require to determine compliance with this section and §493.15(e);

(2) Agree to permit announced and unannounced inspections by HHS in accordance with subpart Q of this part under the following circumstances:

(i) When HHS has substantive reason to believe that the laboratory is being operated in a manner that constitutes an imminent and serious risk to human health.

Interpretive Guidelines §493.35(d)(2)(i)

Consult with your RO for assistance in determining when there is substantive reason to believe that the laboratory is being operated in a manner that constitutes an imminent and serious risk to human health.

An example of a substantive reason to inspect waived testing is if testing personnel are observed cutting urine dipsticks in half. (This violates both the manufacturer's instructions and causes questionable results to be reported.)

(ii) To evaluate complaints from the public.

(iii) On a random basis to determine whether the laboratory is performing tests not listed in §493.15.

Interpretive Guidelines §493.35(d)(2)(ii)-(iii)

See §§6136, 6220 and 6222 (along with the cross reference to Chapter 5) of the SOM for specific procedures regarding complaint investigations and §6174 through §6210 of the SOM for validation surveys.

(iv) To collect information regarding the appropriateness of waiver of tests listed in §493.15.

(e) Denial of application. If HHS determines that the application for a certificate of waiver is to be denied, HHS will--

(1) Provide the laboratory with a written statement of the grounds on which the denial is based and an opportunity for appeal, in accordance with the procedures set forth in subpart R of this part;

(2) Notify a laboratory that has its application for a certificate of waiver denied that it cannot operate as a laboratory under the PHS Act unless the denial is overturned at the conclusion of the administrative appeals process provided by subpart R; and

(3) Notify the laboratory that it is not eligible for payment under the Medicare and Medicaid programs.

§493.37 Requirements for a certificate of waiver

(a) HHS will issue a certificate of waiver to a laboratory only if the laboratory meets the requirements of §493.35.

(b) Laboratories issued a certificate of waiver--

(1) Are subject to the requirements of this subpart and §493.15(e) of subpart A of this part; and

Interpretive Guidelines §493.37(b)(1)

Cite the laboratory's failure to follow manufacturer's instructions at §493.15(e). (Use D1001.)

(2) Must permit announced or unannounced inspections by HHS in accordance with subpart Q of this part.

(c) Laboratories must remit the certificate of waiver fee specified in subpart F of this part.

(d) In accordance with subpart R of this part, HHS will suspend or revoke or limit a laboratory's certificate of waiver for failure to comply with the requirements of this subpart. In addition, failure to meet the requirements of this subpart will result in suspension or denial of payments under Medicare and Medicaid in accordance with subpart R of this part.

Interpretive Guidelines §493.37(d)

See the Adverse Action section of the SOM beginning at §6250 for enforcement procedures.

(e)(1) A certificate of waiver issued under this subpart is valid for no more than 2 years. In the event of a non-compliance determination resulting in HHS action to revoke, suspend, or limit the laboratory's certificate of waiver, HHS will provide the laboratory with a statement of grounds on which the determination of non-compliance is based and offer an opportunity for appeal as provided in subpart R of this part.

(2) If the laboratory requests a hearing within the time specified by HHS, it retains its certificate of waiver or reissued certificate of waiver until a decision is made by an administrative law judge, as specified in subpart R of this part, except when HHS finds that conditions at the laboratory pose an imminent and serious risk to human health.

(3) For laboratories receiving payment from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory of a non-compliance determination even if there has been no appeals decision issued.

(f) A laboratory seeking to renew its certificate of waiver must--

(1) Complete the renewal application prescribed by HHS and return it to HHS not less than 9 months nor more than 1 year before the expiration of the certificate; and

(2) Meet the requirements of §§493.35 and 493.37.

(g) A laboratory with a certificate of waiver that wishes to perform examinations or tests not listed in the waiver test category must meet the requirements set forth in subpart C or subpart D of this part, as applicable.

§493.39 Notification requirements for laboratories issued a certificate of waiver.

Laboratories performing one or more tests listed in §493.15 and no others must notify HHS or its designee--

(a) Before performing and reporting results for any test or examination that is not specified under §493.15 for which the laboratory does not have the appropriate certificate as required in subpart C or subpart D of this part, as applicable; and

(b) Within 30 days of any change(s) in--

(1) Ownership;

(2) Name;

(3) Location; or

(4) Director.

Interpretive Guideline §493.39(a) and (b)

See §§6006 and 6030 of the SOM for instructions on handling a laboratory operating without an appropriate CLIA certificate.

See the section of the SOM regarding The Survey Process beginning at §6100 for instructions on handling changes in ownership, name, location, or director.

Subpart C--Registration Certificate, Certificate for Provider-performed Microscopy Procedures, and Certificate of Compliance

§493.43 Application for registration certificate, certificate for provider-performed microscopy (PPM) procedures, and certificate of compliance.

(a) Filing of application. Except as specified in paragraph (b) of this section, all laboratories performing nonwaived testing must file a separate application for each laboratory location.

(b) Exceptions. (1) Laboratories that are not at a fixed location, that is, laboratories that move from testing site to testing site, such as mobile units providing laboratory testing, health screening fairs, or other temporary testing locations may be covered under the certificate of the designated primary site or home base, using its address.

Interpretive Guidelines §493.43(b)(1)

A mobile unit is a laboratory located within a self-contained vehicle, such as a van. The vehicle moves from location to location to perform laboratory testing activities. All pre-analytic, analytic and post analytic activities are conducted within the confines of the vehicle.

Laboratories with multiple testing sites or mobile laboratories eligible for a single certificate should obtain a separate certificate for each State in which testing is performed.

If a mobile laboratory operates in more than one State and does not obtain a separate certificate from each State, contact the RO to determine which State conducts the inspection.

Each laboratory that moves from testing site to testing site, or has a temporary testing location, should provide the survey agency with the home base or central dispatch phone number so that an updated schedule of the location of testing and the hours of operation can be obtained upon request.

Records may be maintained in the mobile laboratory or at the home base. Reports should reflect the home base address and indicate which mobile unit performed the test.

Mobile vans will be distinguished by the vehicle identification number (VIN #). See SOM §6034 for additional information on mobile laboratories.

(2) Not-for-profit or Federal, State, or local government laboratories that engage in limited (not more than a combination of 15 moderately complex or waived tests per certificate) public health testing may file a single application.

Interpretive Guidelines §493.43(b)(2)

See §6008 of the SOM for the definition of limited public health testing.

See §6008 of the SOM for assistance in determining whether laboratories under the same ownership can file a single application.

(3) Laboratories within a hospital that are located at contiguous buildings on the same campus and under common direction may file a single application or multiple applications for the laboratory sites within the same physical location or street address.

Interpretive Guidelines §493.43(b)(3)

In instances where the main laboratory is certified to perform waived, moderate and/or high complexity tests, the alternate sites may perform testing in all complexities covered by the certificate provided that all other applicable requirements are met (e.g., quality control, personnel).

"Common direction" means that all sites are under one designated director.

"Street address" is the address assigned by the Post Office and is the physical location of the laboratory. The street address may be different from the mailing address, which can be a Post Office box or a billing address. For large hospitals, such as a university campus facility, that may contain laboratories in separate buildings, consult with the RO to determine if the hospital is eligible for a single certificate.

(c) Application format and contents. The application must--(1) Be made to HHS or its designee on a form or forms prescribed by HHS;

- (2) Be signed by an owner, or by an authorized representative of the laboratory who attests that the laboratory will be operated in accordance with the requirements established by the Secretary under section 353 of the Public Health Service Act; and
- (3) Describe the characteristics of the laboratory operation and the examinations and other test procedures performed by the laboratory including--
- (i) The name and total number of test procedures and examinations performed annually (excluding waived tests or tests for quality control, quality assessment or proficiency testing purposes);
 - (ii) The methodologies for each laboratory test procedure or examination performed, or both;
 - (iii) The qualifications (educational background, training, and experience) of the personnel directing and supervising the laboratory and performing the examinations and test procedures.
- (d) *Access and reporting requirements.* All laboratories must make records available and submit reports to HHS as HHS may reasonably require to determine compliance with this section.
-

§493.45 Requirements for a registration certificate.

Laboratories performing only waived tests, PPM procedures, or any combination of these tests, are not required to obtain a registration certificate.

(a) A registration certificate is required-- (1) Initially for all laboratories performing test procedures of moderate complexity (other than the subcategory of PPM procedures) or high complexity, or both; and

(2) For all laboratories that have been issued a certificate of waiver or certificate for PPM procedures that intend to perform tests of moderate or high complexity, or both, in addition to those tests listed in §493.15(c) or specified as PPM procedures.

Interpretive Guidelines §493.45(a)

All facilities performing laboratory testing must have a registration certificate or certificate of waiver prior to performing patient testing.

See §§6006 and 6030 of the SOM for instructions on handling a laboratory operating without an appropriate CLIA certificate.

(b) HHS will issue a registration certificate if the laboratory--

(1) Complies with the requirements of §493.43;

(2) Agrees to notify HHS or its designee within 30 days of any changes in ownership, name, location, director or technical supervisor (laboratories performing high complexity testing only);

(3) Agrees to treat proficiency testing samples in the same manner as it treats patient specimens; and

(4) Remits the fee for the registration certificate, as specified in subpart F of this part.

(c) Prior to the expiration of the registration certificate, a laboratory must--

(1) Remit the certificate fee specified in subpart F of this part;

(2) Be inspected by HHS as specified in subpart Q of this part; and

(3) Demonstrate compliance with the applicable requirements of this subpart and subparts H, J, K, M, and Q of this part.

(d) In accordance with subpart R of this part, HHS will initiate suspension or revocation of a laboratory's registration certificate and will deny the laboratory's application for a certificate of compliance for failure to comply with the requirements set forth in this subpart. HHS may also impose certain alternative sanctions. In addition, failure to meet the requirements of this subpart will result in suspension of payments under Medicare and Medicaid as specified in subpart R of this part.

(e) A registration certificate is--

- (1) Valid for a period of no more than two years or until such time as an inspection to determine program compliance can be conducted, whichever is shorter; and
- (2) Not renewable; however, the registration certificate may be reissued if compliance has not been determined by HHS prior to the expiration date of the registration certificate.
- (f) In the event of a noncompliance determination resulting in an HHS denial of a laboratory's certificate of compliance application, HHS will provide the laboratory with a statement of grounds on which the noncompliance determination is based and offer an opportunity for appeal as provided in subpart R.

Interpretive Guidelines §493.45(f)

See the Appeals section of the SOM beginning at §6300 for instructions on denial of a certificate application.

- (g) If the laboratory requests a hearing within the time specified by HHS, it retains its registration certificate or reissued registration certificate until a decision is made by an administrative law judge as provided in subpart R of this part, except when HHS finds that conditions at the laboratory pose an imminent and serious risk to human health.
- (h) For laboratories receiving payment from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory of denial of the certificate application even if there has been no appeals decision issued.

§493.47 Requirements for a certificate for provider-performed microscopy (PPM) procedures.

- (a) A certificate for PPM procedures is required--
- (1) Initially for all laboratories performing test procedures specified as PPM procedures; and
- (2) For all certificate of waiver laboratories that intend to perform only test procedures specified as PPM procedures in addition to those tests listed in §493.15(c).
- (b) HHS will issue a certificate for PPM procedures if the laboratory--
- (1) Complies with the requirements of §493.43; and
- (2) Remits the fee for the certificate, as specified in subpart F of this part.
- (c) Laboratories issued a certificate for PPM procedures are subject to--
- (1) The notification requirements of §493.53;
- (2) The applicable requirements of this subpart and subparts H, J, K, and M of this part; and
- (3) Inspection only under the circumstances specified under §493.1773 and 493.1775, but are not routinely inspected to determine compliance with the requirements specified in paragraphs (c) (1) and (2) of this section.
- (d) In accordance with subpart R of this part, HHS will initiate suspension, limitation, or revocation of a laboratory's certificate for PPM procedures for failure to comply with the applicable requirements set forth in this subpart. HHS may also impose certain alternative sanctions. In addition, failure to meet the requirements of this subpart may result in suspension of all or part of payments under Medicare and Medicaid, as specified in subpart R of this part.
- (e) A certificate for PPM procedures is valid for a period of no more than 2 years.

§493.49 Requirements for a certificate of compliance.

A certificate of compliance may include any combination of tests categorized as high complexity or moderate complexity or listed in §493.15(c) as waived tests. Moderate complexity tests may include those specified as PPM procedures.

- (a) HHS will issue a certificate of compliance to a laboratory only if the laboratory--
- (1) Meets the requirements of §§493.43 and 493.45;

- (2) Remits the certificate fee specified in subpart F of this part; and
- (3) Meets the applicable requirements of this subpart and subparts H, J, K, M, and Q of this part.
- (b) Laboratories issued a certificate of compliance--
 - (1) Are subject to the notification requirements of §493.51; and
 - (2) Must permit announced or unannounced inspections by HHS in accordance with subpart Q of this part--
 - (i) To determine compliance with the applicable requirements of this part;
 - (ii) To evaluate complaints;
 - (iii) When HHS has substantive reason to believe that tests are being performed, or the laboratory is being operated in a manner that constitutes an imminent and serious risk to human health; and
 - (iv) To collect information regarding the appropriateness of tests listed in §493.15 or tests categorized as moderate complexity (including the subcategory) or high complexity.
- (c) Failure to comply with the requirements of this subpart will result in--
 - (1) Suspension, revocation or limitation of a laboratory's certificate of compliance in accordance with subpart R of this part; and
 - (2) Suspension or denial of payments under Medicare and Medicaid in accordance with subpart R of this part.
- (d) A certificate of compliance issued under this subpart is valid for no more than 2 years.
- (e) In the event of a noncompliance determination resulting in an HHS action to revoke, suspend or limit the laboratory's certificate of compliance, HHS will--
 - (1) Provide the laboratory with a statement of grounds on which the determination of noncompliance is based; and
 - (2) Offer an opportunity for appeal as provided in subpart R of this part. If the laboratory requests a hearing within 60 days of the notice of sanction, it retains its certificate of compliance or reissued certificate of compliance until a decision is made by an administrative law judge (ALJ) as provided in subpart R of this part, except when HHS finds that conditions at the laboratory pose an imminent and serious risk to human health or when the criteria at §493.1840(a) (4) and (5) are met.
- (f) For laboratories receiving payment from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory of a noncompliance determination even if there has been no appeals decision issued.
- (g) A laboratory seeking to renew its certificate of compliance must--
 - (1) Complete and return the renewal application to HHS 9 to 12 months prior to the expiration of the certificate of compliance; and
 - (2) Meet the requirements of §493.43 and paragraphs (a)(2) and (b)(2) of this section.
- (h) If HHS determines that the application for the renewal of a certificate of compliance must be denied or limited, HHS will notify the laboratory in writing of the--
 - (1) Basis for denial of the application; and
 - (2) Opportunity for appeal as provided in subpart R of this part.

Interpretive Guidelines §493.49(h)(2)

See the Appeals section of the SOM beginning at §6300 for instructions on denial of a certificate application.

- (i) If the laboratory requests a hearing within the time period specified by HHS, the laboratory retains its certificate of compliance or reissued certificate of compliance until a decision is made by an ALJ as provided in subpart R, except when HHS finds that conditions at the laboratory pose an imminent and serious risk to human health.
 - (j) For laboratories receiving payment from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory of nonrenewal of the certificate of compliance even if there has been no appeals decision issued.
-

§493.51 Notification requirements for laboratories issued a certificate of compliance.

Laboratories issued a certificate of compliance must meet the following conditions:

- (a) Notify HHS or its designee within 30 days of any change in--
- (1) Ownership;
 - (2) Name;
 - (3) Location;
 - (4) Director; or
 - (5) Technical supervisor (laboratories performing high complexity only).
- (b) Notify HHS no later than 6 months after performing any test or examination within a specialty or subspecialty area that is not included on the laboratory's certificate of compliance, so that compliance with requirements can be determined.
- (c) Notify HHS no later than 6 months after any deletions or changes in test methodologies for any test or examination included in a specialty or subspecialty, or both, for which the laboratory has been issued a certificate of compliance.

Interpretive Guidelines §493.51(c)

See the section of the SOM beginning at §6016 and §6032 for handling changes in ownership, name, location, personnel and test methodology, or additions or deletions of specialties or subspecialties that may result in changes in complexity levels for the laboratory.

See the Adverse Action section of the SOM beginning at §6256 for instructions on handling laboratories that are going out of business or voluntarily withdrawing from all testing.

§493.53 Notification requirements for laboratories issued a certificate for provider-performed microscopy (PPM) procedures.

Laboratories issued a certificate for PPM procedures must notify HHS or its designee--

- (a) Before performing and reporting results for any test of moderate or high complexity, or both, in addition to tests specified as PPM procedures or any test or examination that is not specified under §493.15(c), for which it does not have a registration certificate as required in subpart C or subpart D, as applicable, of this part; and
- (b) Within 30 days of any change in--
- (1) Ownership;
 - (2) Name;
 - (3) Location; or
 - (4) Director.

Interpretive Guidelines §493.53(b)

See the section of the SOM beginning at §6016 and §6032 for handling changes in ownership, name, location, personnel and test methodology, or additions or deletions of specialties or subspecialties that may result in changes in complexity levels for the laboratory.

See the Adverse Action section of the SOM beginning at §6256 for instructions on handling laboratories that are going out of business or voluntarily withdrawing from all testing.

Subpart D--Certificate of Accreditation

§493.55 Application for registration certificate and certificate of accreditation.

(a) Filing of application. A laboratory may be issued a certificate of accreditation in lieu of the applicable certificate specified in subpart B or subpart C of this part provided the laboratory--

(1) Meets the standards of a private non-profit accreditation program approved by HHS in accordance with subpart E; and

Interpretive Guidelines §493.55(a)(1)

When HHS approves accreditation organizations and State licensure programs, the ROs are notified and the approved organizations and programs are published as a notice in the Federal Register.

See the section of the SOM for special procedures for accredited laboratories and CLIA-exempt laboratories beginning at §§6152 and 6210.

(2) Files a separate application for each location, except as specified in paragraph (b) of this section.

(b) Exceptions. (1) Laboratories that are not at fixed locations, that is, laboratories that move from testing site to testing site, such as mobile units providing laboratory testing, health screening fairs, or other temporary testing locations may be covered under the certificate of the designated primary site or home base, using its address.

Interpretive Guidelines §493.55(b)(1)

A mobile unit is a laboratory located within a self-contained vehicle, such as a van. The vehicle moves from location to location to perform laboratory testing activities. All pre-analytic, analytic and post analytic activities are conducted within the confines of the vehicle.

Laboratories with multiple testing sites or mobile laboratories eligible for a single certificate should obtain a separate certificate for each State in which testing is performed.

If a mobile laboratory operates in more than one State and does not obtain a separate certificate from each State, contact the RO to determine which State conducts the inspection.

Each laboratory that moves from testing site to testing site, or has a temporary testing location, should provide the survey agency with the home base or central dispatch phone number so that an updated schedule of the location of testing and the hours of operation can be obtained upon request.

Records may be maintained in the mobile laboratory or at the home base. Reports should reflect the home base address and indicate which mobile unit performed the test.

Mobile vans will be distinguished by the vehicle identification number (VIN #). See §6034 of the SOM for additional information on mobile laboratories.

(2) Not-for-profit or Federal, State, or local government laboratories that engage in limited (not more than a combination of 15 moderately complex or waived tests per certificate) public health testing may file a single application.

Interpretive Guidelines §493.55(b)(2)

See §6008 of the SOM for the definition of limited public health testing.

See §6008 of the SOM for assistance in determining whether laboratories under the same ownership can file a single application.

(3) Laboratories within a hospital that are located at contiguous buildings on the same campus and under common direction may file a single application or multiple applications for the laboratory sites within the same physical location or street address.

Interpretive Guidelines §493.55(b)(3)

"Common direction" means that all sites are under one designated director.

"Street address" is the address assigned by the Post Office and is the physical location of the laboratory. The street address may be different from the mailing address, which can be a Post Office box or a billing address. For large hospitals, such as a university campus facility, that may contain laboratories in separate buildings, consult with the RO to determine if the hospital is eligible for a single certificate.

- (c) Application format and contents. The application must--**
- (1) Be made to HHS on a form or forms prescribed by HHS;**
 - (2) Be signed by an owner or authorized representative of the laboratory who attests that the laboratory will be operated in accordance with the requirements established by the Secretary under section 353 of the Public Health Service Act; and**
 - (3) Describe the characteristics of the laboratory operation and the examinations and other test procedures performed by the laboratory including--**
 - (i) The name and total number of tests and examinations performed annually (excluding waived tests and tests for quality control, quality assurance or proficiency testing purposes);**
 - (ii) The methodologies for each laboratory test procedure or examination performed, or both; and**
 - (iii) The qualifications (educational background, training, and experience) of the personnel directing and supervising the laboratory and performing the laboratory examinations and test procedures.**
- (d) Access and reporting requirements. All laboratories must make records available and submit reports to HHS as HHS may reasonably require to determine compliance with this section.**

§493.57 Requirements for a registration certificate.

A registration certificate is required for all laboratories seeking a certificate of accreditation, unless the laboratory holds a valid certificate of compliance issued by HHS.

Interpretive Guidelines §493.57

See §§6006 and 6030 of the SOM for instructions on handling a laboratory operating without a CLIA certificate.

- (a) HHS will issue a registration certificate if the laboratory--**
- (1) Complies with the requirements of §493.55;**
 - (2) Agrees to notify HHS within 30 days of any changes in ownership, name, location, director, or supervisor (laboratories performing high complexity testing only);**
 - (3) Agrees to treat proficiency testing samples in the same manner as it treats patient specimens; and**
 - (4) Remits the fee for the registration certificate specified in subpart F of this part.**
- (b)(1) The laboratory must provide HHS with proof of accreditation by an approved accreditation program--**
- (i) Within 11 months of issuance of the registration certificate; or**
 - (ii) Prior to the expiration of the certificate of compliance.**
- (2) If such proof of accreditation is not supplied within this timeframe, the laboratory must meet, or continue to meet, the requirements of §493.49.**

(c) In accordance with subpart R of this part, HHS will initiate suspension, revocation, or limitation of a laboratory's registration certificate and will deny the laboratory's application for a certificate of accreditation for failure to comply with the requirements set forth in this subpart. In addition, failure to meet the requirements of this subpart will result in suspension or denial of payments under Medicare and Medicaid as specified in subpart R of this part.

(d) A registration certificate is valid for a period of no more than 2 years. However, it may be reissued if the laboratory is subject to subpart C of this part, as specified in §493.57(b)(2) and compliance has not been determined by HHS before the expiration date of the registration certificate.

(e) In the event that the laboratory does not meet the requirements of this subpart, HHS will--

Interpretive Guidelines §493.57

See the Appeals section of the SOM beginning at §6300 for instructions on denial of a certificate of accreditation application.

- (1) Deny a laboratory's request for certificate of accreditation;
- (2) Notify the laboratory if it must meet the requirements for a certificate as defined in subpart C of this part;
- (3) Provide the laboratory with a statement of grounds on which the application denial is based;
- (4) Offer an opportunity for appeal on the application denial as provided in subpart R of this part. If the laboratory requests a hearing within the time specified by HHS, the laboratory will retain its registration certificate or reissued registration certificate until a decision is made by an administrative law judge as provided in subpart R, unless HHS finds that conditions at the laboratory pose an imminent and serious risk to human health; and
- (5) For those laboratories receiving payment from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory of denial of the request even if there has been no appeals decision issued.

§493.61 Requirements for a certificate of accreditation.

- (a) HHS will issue a certificate of accreditation to a laboratory if the laboratory--
- (1) Meets the requirements of §493.57 or, if applicable, §493.49 of subpart C of this part; and
 - (2) Remits the certificate of accreditation fee specified in subpart F of this part.
- (b) Laboratories issued a certificate of accreditation must--
- (1) Treat proficiency testing samples in the same manner as patient samples;
 - (2) Meet the requirements of §493.63;
 - (3) Comply with the requirements of the approved accreditation program;
 - (4) Permit random sample validation and complaint inspections as required in subpart Q of this part;
 - (5) Permit HHS to monitor the correction of any deficiencies found through the inspections specified in paragraph (b)(4) of this section;

Interpretive Guidelines §493.61(b)(5)

See the section of the SOM regarding Special Procedures for Accredited and CLIA-exempt laboratories beginning at §§6152 and 6200 for procedures on follow-up of correction of deficiencies cited during validation inspections.

- (6) Authorize the accreditation program to release to HHS the laboratory's inspection findings whenever HHS conducts random sample or complaint inspections; and

(7) Authorize its accreditation program to submit to HHS the results of the laboratory's proficiency testing.

(c) A laboratory failing to meet the requirements of this section--

(1) Will no longer meet the requirements of this part by virtue of its accreditation in an approved accreditation program;

(2) Will be subject to full determination of compliance by HHS;

(3) May be subject to suspension, revocation or limitation of the laboratory's certificate of accreditation or certain alternative sanctions; and

(4) May be subject to suspension of payments under Medicare and Medicaid as specified in subpart R.

(d) A certificate of accreditation issued under this subpart is valid for no more than 2 years. In the event of a non-compliance determination as a result of a random sample validation or complaint inspection, a laboratory will be subject to a full review by HHS in accordance with §488.11 of this chapter.

Interpretive Guidelines §493.61(d)

42 CFR §488.11 refers to State survey agency functions.

(e) Failure to meet the applicable requirements of part 493, will result in an action by HHS to suspend, revoke or limit the certificate of accreditation. HHS will--

(1) Provide the laboratory with a statement of grounds on which the determination of noncompliance is based;

(2) Notify the laboratory if it is eligible to apply for a certificate as defined in subpart C of this part; and

(3) Offer an opportunity for appeal as provided in subpart R of this part.

(f) If the laboratory requests a hearing within the time frame specified by HHS--

(1) It retains its certificate of accreditation or reissued certificate of accreditation until a decision is made by an administrative law judge as provided in subpart R of this part, unless HHS finds that conditions at the laboratory pose an imminent and serious risk to human health; and

(2) For those laboratories receiving payments from the Medicare or Medicaid program, such payments will be suspended on the effective date specified in the notice to the laboratory even if there has been no appeals decision issued.

(g) In the event the accreditation organization's approval is removed by HHS, the laboratory will be subject to the applicable requirements of subpart C of this part or §493.57.

Interpretive Guidelines §493.61(g)

Accrediting organizations which lose deemed status are required to notify their participating laboratories. These laboratories must apply for a CLIA certificate.

(h) A laboratory seeking to renew its certificate of accreditation must--

(1) Complete and return the renewal application to HHS 9 to 12 months prior to the expiration of the certificate of accreditation;

(2) Meet the requirements of this subpart; and

(3) Submit the certificate of accreditation fee specified in subpart F of this part.

(i) If HHS determines that the renewal application for a certificate of accreditation is to be denied or limited, HHS will notify the laboratory in writing of--

(1) The basis for denial of the application;

(2) Whether the laboratory is eligible for a certificate as defined in subpart C of this part;

(3) The opportunity for appeal on HHS's action to deny the renewal application for certificate of accreditation as provided in subpart R of this part. If the laboratory requests a hearing within the time frame specified by HHS, it retains its certificate of accreditation or reissued certificate of accreditation until a decision is made by an administrative law judge as provided in subpart R of this part, unless HHS finds that conditions at the laboratory pose an imminent and serious risk to human health; and

(4) Suspension of payments under Medicare or Medicaid for those laboratories receiving payments under the Medicare or Medicaid programs.

§493.63 Notification requirements for laboratories issued a certificate of accreditation.

Laboratories issued a certificate of accreditation must:

(a) Notify HHS and the approved accreditation program within 30 days of any changes in--

- (1) Ownership;**
- (2) Name;**
- (3) Location; or**
- (4) Director.**

(b) Notify the approved accreditation program no later than 6 months after performing any test or examination within a specialty or subspecialty area that is not included in the laboratory's accreditation, so that the accreditation organization can determine compliance and a new certificate of accreditation can be issued.

(c) Notify the accreditation program no later than 6 months after of any deletions or changes in test methodologies for any test or examination included in a specialty or subspecialty, or both, for which the laboratory has been issued a certificate of accreditation.

Interpretive Guidelines §493.63(c)

See the section of the SOM beginning at §6016 and §6032 for handling changes in ownership, name, location, personnel and test methodology, or additions or deletions of specialties or subspecialties that may result in changes in complexity levels for the laboratory.

See the Adverse Action section of the SOM beginning at §6256 for instructions on handling laboratories that are going out of business or voluntarily withdrawing from all testing.

Subpart H--Participation in Proficiency Testing for Laboratories Performing Nonwaived Testing

Subpart H - Guidelines - General

By law, proficiency testing (PT) programs are evaluated initially for CMS approval and annually thereafter for re-approval. After review, Central Office (CO) will issue PT program approvals and/or re-approvals. A listing of these programs with the specialties, subspecialties, and analytes for which they are approved will be provided to ROs. The RO is responsible for disseminating the approved program listing to the States within their region on an annual basis. Address questions related to the currently approved PT programs to the RO.

An approved PT program is a program that has been evaluated and found to be in compliance with the requirements of Subpart I and the applicable sections of Subpart H. When a laboratory experiences problems with PT, it resolves them with the PT program. If a PT program fails to meet the requirements of Subpart I, report all available information to the RO, which discusses the findings with CO. CO renders a decision on the termination or continued approval of the PT program, as appropriate. The Centers for Disease Control and Prevention may be requested by CO to provide technical advise.

D2000

§493.801 Condition: Enrollment and testing of samples

Each laboratory must enroll in a proficiency testing (PT) program that meets the criteria in subpart I of this part and is approved by HHS. The laboratory must enroll in an approved program or programs for each of the specialties and subspecialties for which it seeks certification. The laboratory must test the samples in the same manner as patients' specimens. For laboratories subject to 42 CFR part 493 published on March 14, 1990 (55 FR 9538) prior to September 1, 1992, the rules of this subpart are effective on September 1, 1992. For all other laboratories, the rules of this subpart are effective January 1, 1994.

Interpretive Guidelines §493.801

Each laboratory must determine the extent of patient testing it performs. The laboratory must review the specialty, subspecialties and analytes listed in Subpart I and determine which specialty, subspecialties and analytes they must enroll in to meet this requirement. Enrollment must be in a CMS approved PT program. The surveyor should verify that the laboratory is properly enrolled in an approved PT program.

Note: *If a laboratory has not enrolled for any or all tests that it perform that are listed in Subpart I, cite ONLY D2000, Enrollment and testing of samples; do not cite D2016, Successful Participation.*

PT requirements apply to the non-waived tests listed in Subpart I. PT is not required for waived tests. If a laboratory enrolls and participates in PT for any waived tests, do not review these PT results and do not determine compliance with any other PT requirements. Do not take enforcement action for referral of PT specimens for waived tests.

PT enrollment and participation is required, as applicable, for each certificate other than a Certificate of Waiver. A facility offering testing at more than one site, but the testing is all included under one certificate, must enroll in an approved PT program(s) for the collective tests covered under that certificate, not for each site. A general rule is "PT enrollment per certificate".

Facilities that perform laboratory testing at multiple sites and are certified under one CLIA certificate include the following examples:

- *A hospital with satellite laboratories throughout the hospital;*
- *Different departments of the laboratory;*
- *A hospital that performs point-of-care testing;*
- *Limited public health testing performed by non-profit or Federal, State or local government laboratories; or*
- *Mobile laboratories or temporary testing sites.*

The following examples give instruction and guidance for determining compliance with the PT requirement for enrollment where a specialty, subspecialty or analyte is performed by different methods, specimen types and locations:

- *A laboratory with a single certificate must enroll in an approved PT program for each analyte listed in Subpart I that it performs. When an analyte is performed using different methodologies within the laboratory, only one enrollment is required. After the laboratory has determined which analyte to enroll for, it must participate in PT using its primary method for patient testing during the event. Other methods for the same analyte must be evaluated as required in §493.1236. If the laboratory performs unsuccessfully for an analyte and sanctions are imposed, the sanctions are applicable to the analyte, not to the test methodology. For example, if a laboratory uses three different methods to perform cholesterol measurements, it must participate in PT using the primary method at the time of the PT event. If the laboratory is unsuccessful in PT performance for cholesterol and the CLIA certificate is suspended, limited, or*

revoked for cholesterol, the laboratory would be precluded from performing cholesterol by any test method.

- A laboratory with a single certificate performing testing at multiple sites under that certificate must participate in PT for each analyte listed in Subpart I that is under that certificate. The performance of PT testing events may be alternated between different sites, provided the primary method at the time of the PT event is used to perform the PT. Should the facility not perform successfully for an analyte, that analyte may not be tested at any location under that certificate.
- A multiple site laboratory, which is covered by a single certificate and participates in one PT program per analyte, must be aware that a failure in PT could lead to the revocation of its certificate for all sites, not just the one participating in PT.

When problems occur that cannot be resolved with the instructions in these guidelines, gather all information available and consult with the RO for guidance and resolution.

D2001

§493.801 Condition: Enrollment and testing of samples

(a) Standard: Enrollment. The laboratory must--

(1) Notify HHS of the approved program or programs in which it chooses to participate to meet proficiency testing requirements of this subpart.

(2)(i) Designate the program(s) to be used for each specialty, subspecialty, and analyte or test to determine compliance with this subpart if the laboratory participates in more than one proficiency testing program approved by CMS; and

Interpretive Guidelines §493.801(a)(1)-(a)(2)(i)

Note: These requirements are met when the CMS approved PT program transmits the laboratory enrollment to the CMS PT monitoring system.

D2003

§493.801 Condition: Enrollment and testing of samples

(2)(ii) For those tests performed by the laboratory that are not included in subpart I of this part, a laboratory must establish and maintain the accuracy of its testing procedures, in accordance with §493.1236(c) (1).

Interpretive Guidelines §493.801(a)

During the on-site survey, verify that the laboratory is enrolled in an approved program or programs for all specialty, subspecialties, and tests or analytes listed in Subpart I for which it performs patient testing.

To meet the requirements of this section, it may be necessary for a laboratory to enroll in more than one program to cover all tests listed in Subpart I for which the laboratory performs testing. The approved program in which a laboratory has enrolled may not offer every analyte that the laboratory performs. The laboratory must then enroll in an additional program(s) to cover the testing not included in the first program.

The laboratory must indicate to the PT program which specialty, subspecialty, or analyte it intends the program to grade and score for regulatory purposes. This is particularly necessary when the laboratory subscribes to multiple PT programs that contain the same analyte(s) required for regulatory purposes.

D2004

§493.801 Condition: Enrollment and testing of samples

(a)(3) For each specialty, subspecialty and analyte or test, participate in one approved proficiency testing program or programs, for one year before designating a different program and must notify CMS before any change in designation; and

Interpretive Guidelines §493.801(a)(3)

When a laboratory initially applies for CLIA certification or adds a specialty or subspecialty in the middle of the calendar year, it may change PT programs at the next PT enrollment period.

D2005

§493.801 Condition: Enrollment and testing of samples

(a)(4) Authorize the proficiency testing program to release to HHS all data required to--

Interpretive Guidelines §493.801(a)(4)

Provide laboratories with the appropriate Federal or State Agency address to which PT results must be sent. Laboratories that are accredited by a CMS approved accreditation organization must release all PT data to its accreditation organization.

(i) Determine the laboratory's compliance with this subpart; and

(ii) Make PT results available to the public as required in section 353(f)(3)(F) of the Public Health Service Act.

Probes §493.801(a)-(b)

What procedure or test method was used? Is this a routine test method used in the laboratory? Did routine personnel perform the PT? How often were PT samples tested? How are deviations (if any) justified?

Do the PT results documented in the laboratory work records (worksheet) correlate with the results reported to the PT program?

What is the laboratory's policy for testing patient samples when PT specimens are tested more than once?

Do reports submitted to the PT program provider accurately reflect the procedure (i.e., instrument, method) used in the laboratory?

Check to see if patient samples were reported on the same day that PT samples were tested. (In a small facility, infrequent testing may necessitate the testing of PT samples without patient specimens to ensure that the the PT test results are returned on time.) Did the laboratory use the same procedure for both patient specimens and PT samples?

D2006

§493.801 Condition: Enrollment and testing of samples

(b) Standard: Testing of proficiency testing samples.

The laboratory must examine or test, as applicable, the proficiency testing samples it receives from the proficiency testing program in the same manner as it tests patient specimens.

Interpretive Guidelines §493.801(b)

Review testing records to determine if special handling was given to PT samples. Consider the unique requirements of many PT samples when evaluating "same manner" of testing. The laboratory should document any necessary reconstitution, longer mixing times, unit conversion of results, etc., as required in §493.801(b)(5).

A central laboratory with more than one instrument or methodology for the same test may alternate methods or instruments from one testing event to the next as long as both are routinely used to test patient specimens. All samples for one analyte within a shipment must be tested with the same instrument.

D2007

§493.801 Condition: Enrollment and testing of samples

(b)(1) The samples must be examined or tested with the laboratory's regular patient workload by personnel who routinely perform the testing in the laboratory, using the laboratory's routine methods.

D2009

§493.801 Condition: Enrollment and testing of samples

(b)(1) The individual testing or examining the samples and the laboratory director must attest to the routine integration of the samples into the patient workload using the laboratory's routine methods.

Interpretive Guidelines §493.801(b)(1)

Review records to assure that the analyst performing the testing and the director have signed the attestation statement certifying that PT samples were tested in the same manner as patient specimens. For moderate complexity testing, in accordance with §493.1407(e)(4)(i), the director may delegate the responsibility for signing the attestation statement to a technical consultant meeting the qualifications of §493.1409. For high complexity testing, in accordance with §493.1445(e)(4)(i), the director may delegate the responsibility for signing the attestation statement to a technical supervisor meeting the qualifications of §493.1447.

D2010

§493.801 Condition: Enrollment and testing of samples

(b)(2) The laboratory must test samples the same number of times that it routinely tests patient samples.

D2011

§493.801 Condition: Enrollment and testing of samples

(b)(3) Laboratories that perform tests on proficiency testing samples must not engage in any inter-laboratory communications pertaining to the results of proficiency testing sample(s) until after the date by which the laboratory must report proficiency testing results to the program for the testing event in which the samples were sent. Laboratories with multiple testing sites or separate locations must not participate in any communications or discussions across sites/locations concerning proficiency testing sample results until after the date by which the laboratory must report proficiency testing results to the program.

D2013

§493.801 Condition: Enrollment and testing of samples

(b)(4) The laboratory must not send PT samples or portions of samples to another laboratory for any analysis which it is certified to perform in its own laboratory. Any laboratory that CMS determines intentionally referred its proficiency testing samples to another laboratory for analysis will have its certification revoked for at least one year. Any laboratory that receives proficiency testing samples from another laboratory for testing must notify CMS of the receipt of those samples.

Interpretive Guidelines §493.801(b)(4)

The regulation refers to intentional referral of PT specimens by a laboratory for purposes of using another laboratory's results as its own. A laboratory that routinely performs only presumptive testing or screening methods and refers patient samples to another laboratory for definitive or confirmatory testing or comparison of test results must not refer PT samples to another laboratory for confirmatory testing. A laboratory must only test and report PT specimens to the degree those tests or examinations are performed for in-house patient testing.

Handle allegations of inter-laboratory communications or referral of proficiency testing specimens as a complaint and investigate using the complaint investigation procedures outlined in §6136 of the SOM.

Do not solicit a Plan of Correction from a laboratory when it has been determined that the laboratory intentionally referred its PT samples to another laboratory for analysis and submitted the other laboratory's results as its own. Immediately notify the RO recommending revocation of the certificate (a statutory requirement) and forward to the RO all documentation necessary to support the findings.

D2015

§493.801 Condition: Enrollment and testing of samples

(b)(5) The laboratory must document the handling, preparation, processing, examination, and each step in the testing and reporting of results for all proficiency testing samples. The laboratory must maintain a copy of all records, including a copy of the proficiency testing program report forms used by the laboratory to record proficiency testing results including the attestation statement provided by the PT program, signed by the analyst and the laboratory director, documenting that proficiency testing samples were tested in the same manner as patient specimens, for a minimum of two years from the date of the proficiency testing event.

Interpretive Guidelines §493.801(b)(5)

Review records to assure that the analyst performing the testing and the director have signed the attestation statement certifying that PT samples were tested in the same manner as patient specimens. For moderate complexity testing, in accordance with §493.1407(e)(4)(i), the director may delegate the responsibility for signing the attestation statement to a technical consultant meeting the qualifications of §493.1409. For high complexity testing, in accordance with §493.1445(e)(4)(i), the director may delegate the responsibility for signing the attestation statement to a technical supervisor meeting the qualifications of §493.1447. The signature of the director or technical consultant/supervisor need not be obtained prior to reporting PT results to the PT provider.

(b)(6) PT is required for only the test system, assay, or examination used as the primary method for patient testing during the PT event.

Interpretive Guidelines §493.801(b)(6)

"Primary" means the test system(s), assay(s) or examination(s) routinely used for patient testing at the time of the PT testing event; however, the primary method is determined after the laboratory has chosen the analyte(s) it performs for enrollment.

D2016

§493.803 Condition: Successful participation.

(a) Each laboratory performing nonwaived testing must successfully participate in a proficiency testing program approved by CMS, if applicable, as described in subpart I of this part for each specialty, subspecialty, and analyte or test in which the laboratory is certified under CLIA.

(b) Except as specified in paragraph (c) of this section, if a laboratory fails to participate successfully in proficiency testing for a given specialty, subspecialty, analyte or test, as defined in this section, or fails to take remedial action when an individual fails gynecologic cytology, CMS imposes sanctions, as specified in subpart R of this part.

(c) If a laboratory fails to perform successfully in a CMS-approved proficiency testing program, for the initial unsuccessful performance, CMS may direct the laboratory to undertake training of its personnel or to obtain technical assistance, or both, rather than imposing alternative or principle sanctions except when one or more of the following conditions exists:

(1) There is immediate jeopardy to patient health and safety.

(2) The laboratory fails to provide CMS or a CMS agent with satisfactory evidence that it has taken steps to correct the problem identified by the unsuccessful proficiency testing performance.

(3) The laboratory has a poor compliance history.

Interpretive Guidelines §493.803

Only the PT program has the capability to correct scores. These corrections will be noted in the PT monitoring system as "non-routine" scores.

No single PT enforcement protocol is universally applicable for all situations. Unique circumstances may require special considerations or actions that may not conform to the general approach outlined below. The laboratory's compliance history, its willingness to take remedial actions, and the professional judgment of surveyors, RO CLIA laboratory consultants and enforcement personnel may be factors in determining an appropriate PT enforcement plan.

Careful review of PT performance reports and other available information should always be performed to determine whether the PT results truly represent failed PT. The potential of a PT program data input error or other factors beyond the laboratory's control should be considered. If the laboratory has made a transcription error(s), it is considered erroneous PT result(s).

Absent any special circumstances (which must be documented in the case file), consider verified unsuccessful PT performance to represent unsuccessful PT participation and cite as a condition-level deficiency (use D2016 on the CMS-2567).

NOTE: The CMS PT monitoring system may NOT be used alone to determine unsuccessful participation. Surveyors must verify any unsuccessful participation

indicated in the PT monitoring system. This may be done by reviewing PT results supplied by the approved PT program (they will send copies to the surveyor if requested) or from results sent to the laboratory by the PT program.

If the unsuccessful PT participation is the first occurrence for the laboratory, and there is no immediate jeopardy to patient health or safety, notify the laboratory and require that it seek training of its personnel, obtain the necessary technical assistance to correct the problem causing the unsuccessful participation, or both. SAs may initiate training and/or technical assistance after first obtaining RO concurrence. No onsite review is required to initiate this action.

The laboratory will submit an acceptable plan of remedial action, listing projected completion dates and other pertinent information, for its training and/or technical assistance efforts. Follow-up is necessary to verify that the laboratory has carried out its plan. Satisfactory participation in the next PT event would provide verification that the laboratory's remedial action, training and/or technical assistance were successful. The remedial action plan should demonstrate that the laboratory will correct its problems within 3 months, although special circumstances may be considered. When a laboratory refuses to take acceptable training and/or technical assistance actions (including failure to submit an acceptable plan of remedial action, or failure to complete its plan), sanction action will be initiated.

When the unsuccessful PT participation is not the first such occurrence for the laboratory, and there is no issue of immediate jeopardy, cite as a condition-level deficiency and take appropriate enforcement action. For immediate jeopardy cases the procedures in Subpart R apply. For non-immediate jeopardy situations, enforcement procedures should be completed within 90 days from the date that the unsuccessful PT was first identified. In immediate jeopardy situations, enforcement procedures should be completed within 23 days from the date unsuccessful participation of PT is first identified.

Example:

A laboratory scores 60% on a testing event in mycobacteriology. On the next testing event, the laboratory fails to participate in mycobacteriology. The citations are §§493.825(b), 493.825(e), and 493.803.

Example:

A laboratory scores 60% on uric acid PT samples. On the next testing event, the laboratory scores 40% on the same analyte. The citations are §§493.841(a), 493.841(f), and 493.803. When recommending to the RO that a laboratory be subject to sanctions, submit copies of the laboratory's testing event or analyte score(s) that were unsatisfactory and the correct responses provided by the PT program. Also, enclose copies of any correspondence sent to or received by the laboratory concerning its PT performance.

When recommending to the RO that a laboratory be subject to sanctions, submit copies of the laboratory's testing event or analyte score(s) that were unsatisfactory and the correct responses provided by the PT program. Also, enclose copies of any correspondence sent or received by the laboratory concerning its PT performance.

D2017

§493.807 Condition: Reinstatement of laboratories performing nonwaived testing after failure to participate

(a) If a laboratory's certificate is suspended or limited or its Medicare or Medicaid approval is cancelled or its Medicare or Medicaid payments are suspended because it fails to participate successfully in proficiency testing for one or more specialties, subspecialties, analyte or test, or voluntarily withdraws its certification under CLIA for the failed specialty, subspecialty, or analyte, the laboratory must then demonstrate sustained satisfactory performance on two consecutive proficiency testing events, one of which may be on site, before CMS will consider it for reinstatement for certification and Medicare or Medicaid approval in that specialty, subspecialty, analyte or test.

D2018

§493.807 Condition: Reinstatement of laboratories performing nonwaived testing

(b) The cancellation period for Medicare and Medicaid approval or period for suspension of Medicare or Medicaid payments or suspension or limitation of certification under CLIA for the failed specialty, subspecialty, or analyte or test is for a period of not less than six months from the date of cancellation, limitation or suspension of the CLIA certificate.

Proficiency Testing by Specialty and Subspecialty for Laboratories Performing Non-Waived Tests

§493.821 Condition: Microbiology.

The specialty of microbiology includes, for purposes of proficiency testing, the subspecialties of bacteriology, mycobacteriology, mycology, parasitology and virology.

D2020

§493.823 Standard; Bacteriology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2021

§493.823 Standard; Bacteriology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

- (1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;
 - (2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and
 - (3) The laboratory participated in the previous two proficiency testing events.
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D2025

§493.823 Standard; Bacteriology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2026

§493.823 Standard; Bacteriology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) Remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2028

§493.823 Standard; Bacteriology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2029

§493.825 Standard; Mycobacteriology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2030

§493.825 Standard; Mycobacteriology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2034

§493.825 Standard; Mycobacteriology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2035

§493.825 Standard; Mycobacteriology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) Remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2037

§493.825 Standard; Mycobacteriology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2038

§493.827 Standard; Mycology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2039

§493.827 Standard; Mycology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2043

§493.827 Standard; Mycology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2044

§493.827 Standard; Mycology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) Remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2046

§493.827 Standard; Mycology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2047

§493.829 Standard; Parasitology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2048

§493.829 Standard; Parasitology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2052

§493.829 Standard; Parasitology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2053

§493.829 Standard; Parasitology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) Remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2055

§493.829 Standard; Parasitology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2056

§493.831 Standard; Virology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2057

§493.831 Standard; Virology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2061

§493.831 Standard; Virology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2062

§493.831 Standard; Virology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unsatisfactory testing events, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2064

§493.831 Standard; Virology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

§493.833 Condition: Diagnostic immunology.

The specialty of diagnostic immunology includes for purposes of proficiency testing the subspecialties of syphilis serology and general immunology.

D2066

§493.835 Standard; Syphilis serology.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2067

§493.835 Standard; Syphilis serology.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2071

§493.835 Standard; Syphilis serology.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2072

§493.835 Standard; Syphilis serology.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2074

§493.835 Standard; Syphilis serology.

(e) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2075

§493.837 Standard; General immunology.

Interpretive Guidelines: §493.837

Analytes or tests for which laboratory PT performance is to be evaluated:

*Alpha-1 antitrypsin
Alpha-fetoprotein (tumor marker)
Antinuclear antibody
Antistreptolysin O – quantitative
Anti-human immunodeficiency virus (HIV)
Complement C3
Complement C4
Hepatitis markers (HBsAg, anti-HBc, HBeAg)
IgA
IgG
IgE
IgM
Infectious mononucleosis
Rheumatoid factor
Rubella*

Note: If a laboratory performs both a quantitative and a qualitative procedure of a test or analyte, it may choose which to enroll in to fulfill the enrollment requirement. It need not enroll in both quantitative and qualitative PT for the same analyte.

(a) Failure to attain a score of at least 80 percent of acceptable responses for each analyte in each testing event is unsatisfactory analyte performance for the testing event.

D2076

§493.837 Standard; General immunology.

(b) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2077

§493.837 Standard; General immunology.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2081

§493.837 Standard; General immunology.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2082

§493.837 Standard; General immunology

(e)(1) For any unsatisfactory analyte or test performance or testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2084

§493.837 Standard; General immunology

(f) Failure to achieve satisfactory performance for the same analyte or test in two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2085

§493.837 Standard; General immunology

(g) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

§493.839 Condition: Chemistry.

The specialty of chemistry includes for the purposes of proficiency testing the subspecialties of routine chemistry, endocrinology, and toxicology.

Analytes or tests for which laboratory PT performance is to be evaluated which include serum, plasma or blood samples:

Alanine aminotransferase (ALT/SGPT)
Albumin
Alkaline phosphatase
Amylase
Aspartate aminotransferase (AST/SGOT)
Bilirubin, total
Blood gas (pH, pO₂, and pCO₂)
Calcium, total
Chloride
Cholesterol, total
Cholesterol, high density lipoprotein
Creatine kinase
Creatine kinase isoenzymes
Creatinine
Glucose (Excluding measurements on devices cleared by FDA specifically for home use)
Iron, total
Lactate dehydrogenase (LDH)
LDH isoenzymes
Magnesium
Potassium
Sodium
Total Protein
Triglycerides
Urea Nitrogen
Uric Acid

D2087

§493.841 Standard; Routine chemistry.

(a) Failure to attain a score of at least 80 percent of acceptable responses for each analyte in each testing event is unsatisfactory analyte performance for the testing event.

D2088

§493.841 Standard; Routine chemistry.

(b) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2089

§493.841 Standard; Routine chemistry.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2093

§493.841 Standard; Routine chemistry.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2094

§493.841 Standard; Routine chemistry.

(e)(1) For any unsatisfactory analyte or test performance or testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2096

§493.841 Standard; Routine chemistry.

(f) Failure to achieve satisfactory performance for the same analyte or test in two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2097

§493.841 Standard; Routine chemistry.

(g) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2098

§493.843 Standard; Endocrinology.

Analytes or tests for which laboratory PT performance is to be evaluated which include serum, plasma, blood, or urine:

Cortisol
Free Thyroxine
Human Chorionic Gonadotropin (Excluding color comparison tests for urine specimens)
T₃ Uptake
Triiodothyronine
Thyroid-stimulating hormone
Thyroxine

Note: If the laboratory performs the same analyte on different specimen types, it may choose which specimen type to enroll in PT. The laboratory need not enroll for each specimen type of the same analyte.

(a) Failure to attain a score of at least 80 percent of acceptable responses for each analyte in each testing event is unsatisfactory analyte performance for the testing event.

D2099

§493.843 Standard; Endocrinology.

(b) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2100

§493.843 Standard; Endocrinology.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

- (1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;**
 - (2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and**
 - (3) The laboratory participated in the previous two proficiency testing events.**
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D2104

§493.843 Standard; Endocrinology.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2105

§493.843 Standard; Endocrinology.

(e)(1) For any unsatisfactory analyte or test performance or testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2107

§493.843 Standard; Endocrinology.

(f) Failure to achieve satisfactory performance for the same analyte or test in two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2108

§493.843 Standard; Endocrinology.

(g) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2109

§493.845 Standard; Toxicology.

Analytes or tests for which laboratory PT performance is to be evaluated which include serum, plasma, or blood:

Alcohol (blood)
Blood lead
Carbamazepine
Digoxin
Ethosuximide
Gentamicin
Lithium
Phenobarbital
Phenytoin
Primidone
Procainamide (and metabolite)
Quinidine
Theophylline

Tobramycin
Valproic Acid

(a) Failure to attain a score of at least 80 percent of acceptable responses for each analyte in each testing event is unsatisfactory analyte performance for the testing event.

D2110

§493.845 Standard; Toxicology.

(b) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2111

§493.845 Standard; Toxicology.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

- (1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;
 - (2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and
 - (3) The laboratory participated in the previous two proficiency testing events.
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D2115

§493.845 Standard; Toxicology.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2116

§493.845 Standard; Toxicology.

(e)(1) For any unsatisfactory analyte or test performance or testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2118

§493.845 Standard; Toxicology.

(f) Failure to achieve satisfactory performance for the same analyte or test in two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2119

§493.845 Standard; Toxicology.

(g) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

§493.849 Condition: Hematology.

The specialty of hematology, for the purpose of proficiency testing, is not subdivided into subspecialties of testing.

Analytes or tests for which laboratory PT performance is to be evaluated:

Cell identification or white blood cell differential (chosen by the laboratory)
Erythrocyte count
Hematocrit (excluding spun microhematocrit)
Hemoglobin
Leukocyte count
Platelet count
Fibrinogen
Partial thromboplastin time
Prothrombin time

D2121

§493.851 Standard; Hematology.

(a) Failure to attain a score of at least 80 percent of acceptable responses for each analyte in each testing event is unsatisfactory analyte performance for the testing event.

D2122

§493.851 Standard; Hematology.

(b) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2123

§493.851 Standard; Hematology.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.
Consideration may be given to those laboratories failing to participate in a testing event only if--

- (1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;
- (2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and
- (3) The laboratory participated in the previous two proficiency testing events.
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D2127

§493.851 Standard; Hematology.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2128

§493.851 Standard; Hematology.

(e)(1) For any unsatisfactory analyte or test performance or testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2130

§493.851 Standard; Hematology.

(f) Failure to achieve satisfactory performance for the same analyte in two consecutive events or two out of three consecutive testing events is unsuccessful performance.

D2131

§493.851 Standard; Hematology.

(g) Failure to achieve an overall testing event score of satisfactory performance for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

§493.853 Condition: Pathology.

The specialty of pathology includes, for purposes of proficiency testing, the subspecialty of cytology limited to gynecologic examinations.

D2132

§493.855 Standard; Cytology: gynecologic examinations.

To participate successfully in a cytology proficiency testing program for gynecologic examinations (Pap smears), the laboratory must meet the requirements of paragraphs (a) through (c) of this section.

D2133

§493.855 Standard; Cytology: gynecologic examinations.

(a) The laboratory must ensure that each individual engaged in the examination of gynecologic preparations is enrolled in a proficiency testing program approved by CMS by January 1, 1995, if available in the State in which he or she is employed.

D2134

§493.855 Standard; Cytology: gynecologic examinations.

The laboratory must ensure that each individual is tested at least once per year and obtains a passing score.

To ensure this annual testing of individuals, an announced or unannounced testing event will be conducted on-site in each laboratory at least once each year. Laboratories will be notified of the time of each announced on-site testing event at least 30 days prior to each event. Additional testing events will be conducted as necessary in each State or region for the purpose of testing individuals who miss the on-site testing event and for retesting individuals as described in paragraph (b) of this section.

D2136

§493.855 Standard; Cytology: gynecologic examinations.

(b) The laboratory must ensure that each individual participates in an annual testing event that involves the examination of a 10-slide test set as described in §493.945.

D2137

§493.855 Standard; Cytology: gynecologic examinations.

Individuals who fail this testing event are retested with another 10-slide test set as described in paragraphs (b)(1) and (b)(2) of this section.

D2138

§493.855 Standard; Cytology: gynecologic examinations.

Individuals who fail this second test are subsequently retested with a 20-slide test set as described in paragraphs (b)(2) and (b)(3) of this section. Individuals are given not more than 2 hours to complete a 10-slide test and not more than 4 hours to complete a 20-slide test.

D2141

§493.855 Standard; Cytology: gynecologic examinations.

Unexcused failure to appear by an individual for a retest will result in test failure with resulting remediation and limitations on slide examinations as specified in (b)(1), (b)(2), and (b)(3) of this section.

D2142

§493.855 Standard; Cytology: gynecologic examinations.

(1) An individual is determined to have failed the annual testing event if he or she scores less than 90 percent on a 10-slide test set.

D2143

§493.855 Standard; Cytology: gynecologic examinations.

For an individual who fails an annual proficiency testing event, the laboratory must schedule a retesting event which must take place not more than 45 days after receipt of the notification of failure.

D2144

§493.855 Standard; Cytology: gynecologic examinations.

(2) An individual is determined to have failed the second testing event if he or she scores less than 90 percent on a 10-slide test set.

D2145

§493.855 Standard; Cytology: gynecologic examinations.

For an individual who fails a second testing event, the laboratory must provide him or her with documented, remedial training and education in the area of failure, and

D2146

§493.855 Standard; Cytology: gynecologic examinations.

must assure that all gynecologic slides evaluated subsequent to the notice of failure are reexamined until the individual is again retested with a 20-slide test set and scores at least 90 percent.

D2147

§493.855 Standard; Cytology: gynecologic examinations.

Reexamination of slides must be documented.

D2148

§493.855 Standard; Cytology: gynecologic examinations.

(3) An individual is determined to have failed the third testing event if he or she scores less than 90 percent on a 20-slide test set.

D2149

§493.855 Standard; Cytology: gynecologic examinations.

An individual who fails the third testing event must cease examining gynecologic slide preparations immediately upon notification of test failure and

D2150

§493.855 Standard; Cytology: gynecologic examinations.

may not resume examining gynecologic slides until the laboratory assures that the individual obtains at least 35 hours of documented, formally structured, continuing education in diagnostic cytopathology that focuses on the examination of gynecologic preparations, and until he or she is retested with a 20-slide test set and scores at least 90 percent.

§493.855 Standard; Cytology: gynecologic examinations.

(c) If a laboratory fails to ensure that individuals are tested or those who fail a testing event are retested, or fails to take required remedial actions as described in paragraphs (b)(1), (b)(2) or (b)(3) of this section, CMS will initiate intermediate sanctions or limit the laboratory's certificate to exclude gynecologic cytology testing under CLIA, and, if applicable, suspend the laboratory's Medicare and Medicaid payments for gynecologic cytology testing in accordance with subpart R of this part.

§493.857 Condition: Immunohematology.

The specialty of immunohematology includes four subspecialties for the purposes of proficiency testing: ABO group and D (Rho) typing; unexpected antibody detection; compatibility testing; and antibody identification.

Analytes or tests for which laboratory PT performance is to be evaluated:

ABO group (excluding subgroups)

D(Rho) typing

Unexpected antibody detection

Compatibility testing

Antibody identification

D2153

§493.859 Standard; ABO group and D (Rho) typing.

(a) Failure to attain a score of at least 100 percent of acceptable responses for each analyte or test in each testing event is unsatisfactory analyte performance for the testing event.

D2154

§493.859 Standard; ABO group and D (Rho) typing.

(b) Failure to attain an overall testing event score of at least 100 percent is unsatisfactory performance.

D2155

§493.859 Standard; ABO group and D (Rho) typing.

(c) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2159

§493.859 Standard; ABO group and D (Rho) typing.

(d) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2160

§493.859 Standard; ABO group and D (Rho) typing.

(e)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unacceptable analyte or unsatisfactory testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2162

§493.859 Standard; ABO group and D (Rho) typing.

(f) Failure to achieve satisfactory performance for the same analyte in two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2163

§493.859 Standard; ABO group and D (Rho) typing.

(g) Failure to achieve an overall testing event score of satisfactory for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2164

§493.861 Standard; Unexpected antibody detection.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2165

§493.861 Standard; Unexpected antibody detection.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2169

§493.861 Standard; Unexpected antibody detection.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2170

§493.861 Standard; Unexpected antibody detection.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unsatisfactory testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2172

§493.861 Standard; Unexpected antibody detection.

(e) Failure to achieve an overall testing event score of satisfactory for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2173

§493.863 Standard; Compatibility testing.

(a) Failure to attain an overall testing event score of at least 100 percent is unsatisfactory performance.

D2174

§493.863 Standard; Compatibility testing.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

- (1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;
 - (2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and
 - (3) The laboratory participated in the previous two proficiency testing events.
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D2178

§493.863 Standard; Compatibility testing.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2179

§493.863 Standard; Compatibility testing.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unsatisfactory testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2181

§493.863 Standard; Compatibility testing.

(e) Failure to achieve an overall testing event score of satisfactory for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

D2182

§493.865 Standard; Antibody identification.

(a) Failure to attain an overall testing event score of at least 80 percent is unsatisfactory performance.

D2183

§493.865 Standard; Antibody identification.

(b) Failure to participate in a testing event is unsatisfactory performance and results in a score of 0 for the testing event.

Consideration may be given to those laboratories failing to participate in a testing event only if--

(1) Patient testing was suspended during the time frame allotted for testing and reporting proficiency testing results;

(2) The laboratory notifies the inspecting agency and the proficiency testing program within the time frame for submitting proficiency testing results of the suspension of patient testing and the circumstances associated with failure to perform tests on proficiency testing samples; and

(3) The laboratory participated in the previous two proficiency testing events.

D2187

§493.865 Standard; Antibody identification.

(c) Failure to return proficiency testing results to the proficiency testing program within the time frame specified by the program is unsatisfactory performance and results in a score of 0 for the testing event.

D2188

§493.865 Standard; Antibody identification.

(d)(1) For any unsatisfactory testing event for reasons other than a failure to participate, the laboratory must undertake appropriate training and employ the technical assistance necessary to correct problems associated with a proficiency testing failure.

(2) For any unsatisfactory testing event score, remedial action must be taken and documented, and the documentation must be maintained by the laboratory for two years from the date of participation in the proficiency testing event.

D2190

§493.865 Standard; Antibody identification.

(e) Failure to identify the same antibody in two consecutive or two out of three consecutive testing events is unsuccessful performance.

D2191

§493.865 Standard; Antibody identification.

(f) Failure to achieve an overall testing event score of satisfactory for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

**Subpart M--Personnel for Nonwaived Testing
(Rev. 32, 02-13-04)**

§493.1351 General.

This subpart consists of the personnel requirements that must be met by laboratories performing moderate complexity testing, PPM procedures, high complexity testing, or any combination of these tests.

Laboratories Performing Provider-Performed Microscopy (PPM) Procedures

§493.1353 Scope.

In accordance with §493.19(b), the moderate complexity procedures specified as PPM procedures are considered such only when personally performed by a health care provider during a patient visit in the context of a physical examination. PPM procedures are subject to the personnel requirements in §§493.1355 through 493.1365.

Interpretive Guidelines §493.1353

PPM procedures are exempt from routine inspections only when performed under the auspices of a Certificate of Provider Performed Microscopy Procedures.

D5980

§493.1355 Condition: Laboratories performing PPM procedures; laboratory director.

The laboratory must have a director who meets the qualification requirements of §493.1357 and provides overall management and direction in accordance with §493.1359.

D5981

§493.1357 Standard; laboratory director qualifications.

The laboratory director must be qualified to manage and direct the laboratory personnel and the performance of PPM procedures as specified in §493.19(c) and must be eligible to be an operator of a laboratory within the requirements of subpart R of this part.

(a) The laboratory director must possess a current license as a laboratory director issued by the State in which the laboratory is located, if the licensing is required.

(b) The laboratory director must meet one of the following requirements:

(b)(1) Be a physician, as defined in §493.2.

(b)(2) Be a midlevel practitioner, as defined in §493.2, authorized by a State to practice independently in the State in which the laboratory is located.

(b)(3) Be a dentist, as defined in §493.2.

D5983

§493.1359 Standard; PPM laboratory director responsibilities.

The laboratory director is responsible for the overall operation and administration of the laboratory, including the prompt, accurate, and proficient reporting of test results. The laboratory director must--

D5985

§493.1359 Standard; PPM laboratory director responsibilities.

(a) Direct no more than five laboratories; and

D5987

§493.1359 Standard; PPM laboratory director responsibilities.

(b) Ensure that any procedure listed under §493.19(c)--

(b)(1) Is personally performed by an individual who meets the qualification requirements in §493.1363; and

(b)(2) Is performed in accordance with applicable requirements in subparts H, J, K, and M of this part.

D5990

§493.1361 Condition: Laboratories performing PPM procedures; testing personnel.

The laboratory must have a sufficient number of individuals who meet the qualification requirements of §493.1363 to perform the functions specified in §493.1365 for the volume and complexity of testing performed.

D5991

§493.1363 Standard; PPM testing personnel qualifications.

Each individual performing PPM procedures must--

(a) Possess a current license issued by the State in which the laboratory is located if the licensing is required; and

(b) Meet one of the following requirements:

(b)(1) Be a physician, as defined in §493.2.

(b)(2) Be a midlevel practitioner, as defined in §493.2, under the supervision of a physician or in independent practice if authorized by the State in which the laboratory is located.

(b)(3) Be a dentist as defined in §493.2 of this part.

D5993

§493.1365 Standard; PPM testing personnel responsibilities.

The testing personnel are responsible for specimen processing, test performance, and for reporting test results. Any PPM procedure must be--

(a) Personally performed by one of the following practitioners:

(a)(1) A physician during the patient's visit on a specimen obtained from his or her own patient or from a patient of a group medical practice of which the physician is a member or employee.

(a)(2) A midlevel practitioner, under the supervision of a physician or in independent practice if authorized by the State in which the laboratory is located, during the patient's visit on a specimen obtained from his or her own patient or from the patient of a clinic, group medical practice, or other health care provider, in which the midlevel practitioner is a member or an employee.

(a)(3) A dentist during the patient's visit on a specimen obtained from his or her own patient or from a patient of a group dental practice of which the dentist is a member or an employee; and

D5995

§493.1365 Standard; PPM testing personnel responsibilities.

(b) Performed using a microscope limited to a brightfield or a phase/contrast microscope.

D6000

Laboratories Performing Moderate Complexity Testing

§493.1403 Condition: Laboratories performing moderate complexity testing; laboratory director.

The laboratory must have a director who meets the qualification requirements of §493.1405 of this subpart and provides overall management and direction in accordance with §493.1407 of this subpart.

Interpretative Guidelines §493.1403:

The Condition: laboratory director is not met when the laboratory director:

- Position is not filled;
- Is not qualified; or
- Does not fulfill the laboratory director's responsibilities.

An individual qualified as laboratory director may not qualify as a technical consultant in a particular specialty or subspecialty unless he or she has the required testing experience.

D6001

§493.1405 Standard; Laboratory director qualifications.

The laboratory director must be qualified to manage and direct the laboratory personnel and the performance of moderate complexity tests and

Interpretative Guidelines §493.1405

Section 353(i)(3) of the PHS Act states "No person who has owned or operated a laboratory which has had its certificate revoked may, within 2 years of the revocation of the certificate, own or operate a laboratory for which a certificate has been issued under this section."

D6002

§493.1405 Standard; Laboratory director qualifications.

must be eligible to be an operator of a laboratory within the requirements of subpart R of this part.

D6003

§493.1405 Standard; Laboratory director qualifications.

a) The laboratory director must possess a current license as a laboratory director issued by the State in which the laboratory is located, if such licensing is required; and

Interpretative Guidelines §493.1405(a)

The term "State" as used in this provision, includes the District of Columbia, the Commonwealth of Puerto Rico, the Commonwealth of Northern Mariana Islands, the Virgin Islands, Guam and American Samoa.

(b) The laboratory director must--

(b)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(b)(1)(ii) Be certified in anatomic or clinical pathology, or both, by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1405(b)(1)(ii)

"Board certified" means the individual has completed all the designated board's requirements, including the examination. If the director is named in a current edition of "The Official American Board of Medical Specialties (ABMS) Directory of Board Certified Medical Specialists (published by ABMS by Elsevier, 11830 Westline Industrial Drive, St. Louis, Missouri 63146, 1-866-856-8075) as appropriately board certified, this may be accepted as evidence of certification without needing further documentation. You may make a notation of this in the laboratory's file.

Qualifications that are equivalent for certification include board eligibility (i.e., the individual meets all education, training or experience requirements to take the examination, but has not actually taken and successfully completed the examination.) An individual who wishes to qualify as a director must supply evidence of this eligibility status. The designated boards, upon request, send a letter to the individual confirming his/her eligibility status. Note that some boards set time restrictions for taking the examination. For purposes of the regulations, the individual must meet the education, training or experience required by the board to be eligible to take the examination and must have confirmation of eligibility status.

(b)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(b)(2)(ii) Have had laboratory training or experience consisting of:

Interpretative Guidelines §493.1405(b)(2)(ii)

The type of experience required under this regulation is clinical in nature. This means directing or supervising personnel who examine and perform tests on human specimens for the purpose of providing information that is used in diagnosing, treating, and monitoring a patient's condition. This experience may include the laboratory director personally examining and performing tests on patient specimens. Patient or medically oriented experience, which is defined as the ordering of tests and interpreting and applying the results of these tests in diagnosing and treating a patient's illness, is unacceptable to meet the requirement for laboratory training or experience.

The laboratory director should have documentation, e.g., signed procedure manuals, test reports, worksheets and workcards, that indicates the director assumes the responsibilities in §493.1407.

Teaching experience directly related to a medical technology program, clinical laboratory sciences program, or a clinical laboratory section of a residency program is considered

acceptable experience. Research experience is also acceptable experience if it is obtained while performing tests on human specimens.

**(b)(2)(ii)(A) At least one year directing or supervising non-waived laboratory testing; or
(b)(2)(ii)(B) Beginning September 1, 1993, have at least 20 continuing medical education credit hours in laboratory practice commensurate with the director responsibilities defined in §493.1407; or**

Interpretative Guidelines §493.1405(b)(2)(ii)(B)

The 20 CMEs must be obtained prior to qualifying as a laboratory director. The CME courses must encompass preanalytic, analytic, and postanalytic phases of testing, and be of such quality as to provide the physician with education equivalent to the experience described in §493.1405(b)(2)(ii)(A). Courses related to laboratory payment and CPT coding would not fulfill this requirement.

CME courses are to be accredited by, or meet the same criteria as the Accreditation Council for Continuing Medical Education (ACCME), and should be designated as American Medical Association Physician's Recognition Award (AMA PRA) Category 1 credits.

Obtain a list of ACCME-accredited providers from ACCME to ascertain which providers' CMEs encompass preanalytic, analytic, and postanalytic phases associated with fulfilling the responsibilities of the laboratory director. A list of ACCME-accredited providers (for CME's) can be accessed and contacted via the Internet at <http://www.accme.org>

(b)(2)(ii)(C) Laboratory training equivalent to paragraph (b)(2)(ii)(B) of this section obtained during medical residency. (For example, physicians certified either in hematology or hematology and medical oncology by the American Board of Internal Medicine); or

Interpretative Guidelines §493.1405(b)(2)(ii)(C)

The residency program should provide the director the knowledge in principles and theories of laboratory practice including: quality control and quality assessment, proficiency testing, the phase of the total process (i.e., preanalytic, analytic and postanalytic), as well as, general laboratory systems, facility administration, and development and implementation of personnel policy and procedure manuals. This training should also include hands-on laboratory testing.

(b)(3) Hold an earned doctoral degree in a chemical, physical, biological, or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1405(b)(3)

See §493.2 for the definition of and guidance for accredited institution.

(b)(3)(i) Be certified by the American Board of Medical Microbiology, the American Board of Clinical Chemistry, the American Board of Bioanalysis, or the American Board of Medical Laboratory Immunology; or

(b)(3)(ii) Have had at least one year experience directing or supervising non-waived laboratory testing;

(b)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution;

(b)(4)(ii) Have at least one year of laboratory training or experience, or both in non-waived testing; and

(b)(4)(iii) In addition, have at least one year of supervisory laboratory experience in non-waived testing; or

(b)(5)(i) Have earned a bachelor's degree in a chemical, physical, or biological science or medical technology from an accredited institution;

- (b)(5)(ii) Have at least 2 years of laboratory training or experience, or both in non-waived testing; and
- (b)(5)(iii) In addition, have at least 2 years of supervisory laboratory experience in non-waived testing;
- (b)(6) Be serving as a laboratory director and must have previously qualified or could have qualified as a laboratory director under §493.1406; or

Interpretative Guidelines §493.1405(b)(6)

For tests of moderate complexity, individuals qualify as laboratory directors, if on February 28, 1992, they previously qualified, or could have qualified under the Federal regulations, published on March 14, 1990, as a laboratory director. After February 28, 1992, individuals must meet the requirements at §§493.1405(b)(1)-(5) to qualify as a laboratory director, unless the individual can demonstrate compliance with §493.1405(b)(6), (that is, on February 28, 1992, he or she could have qualified as a laboratory director under Federal regulations published on March 14, 1990).

- (b)(7) On or before February 28, 1992, qualified under State law to direct a laboratory in the State in which the laboratory is located.

§493.1406 Standard; Laboratory director qualifications on or before February 28, 1992.

The laboratory director must be qualified to manage and direct the laboratory personnel and test performance.

- (a) The laboratory director must possess a current license as a laboratory director issued by the State, if such licensing exists; and

(b) The laboratory director must:

- (b)(1) Be a physician certified in anatomical or clinical pathology (or both) by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification;

(b)(2) Be a physician who:

- (b)(2)(i) Is certified by the American Board of Pathology or the American Osteopathic Board of Pathology in at least one of the laboratory specialties; or

(b)(2)(ii) Is certified by the American Board of Medical Microbiology, the American Board of Clinical Chemistry, the American Board of Bioanalysis, or other national accrediting board in one of the laboratory specialties; or

(b)(2)(iii) Is certified by the American Society of Cytology to practice cytopathology or possesses qualifications that are equivalent to those required for such certification; or

(b)(2)(iv) Subsequent to graduation, has had 4 or more years of full-time general laboratory training and experience of which at least 2 years were spent acquiring proficiency in one of the laboratory specialties;

(b)(3) For the subspecialty of oral pathology only, be certified by the American Board of Oral Pathology, American Board of Pathology or the American Osteopathic Board of Pathology or possesses qualifications that are equivalent to those required for certification;

(b)(4) Hold an earned doctoral degree from an accredited institution with a chemical, physical, or biological science as a major subject and

(b)(4)(i) Is certified by the American Board of Medical Microbiology, the American Board of Clinical Chemistry, the American Board of Bioanalysis, or other national accrediting board acceptable to HHS in one of the laboratory specialties; or

(b)(4)(ii) Subsequent to graduation, has had 4 or more years of full-time general laboratory training and experience of which at least 2 years were spent acquiring proficiency in one of the laboratory specialties;

(b)(5) With respect to individuals first qualifying before July 1, 1971, have been responsible for the direction of a laboratory for 12 months between July 1, 1961, and January 1, 1968, and, in addition, either:

- (b)(5)(i) Was a physician and subsequent to graduation had at least 4 years of pertinent full-time laboratory experience;
- (b)(5)(ii) Held a master's degree from an accredited institution with a chemical, physical, or biological science as a major subject and subsequent to graduation had at least 4 years of pertinent full-time laboratory experience;
- (b)(5)(iii) Held a bachelor's degree from an accredited institution with a chemical, physical, or biological science as a major subject and subsequent to graduation had at least 6 years of pertinent full-time laboratory experience; or
- (b)(5)(iv) Achieved a satisfactory grade through an examination conducted by or under the sponsorship of the U.S. Public Health Service on or before July 1, 1970; or
- (b)(6) Qualify under State law to direct the laboratory in the State in which the laboratory is located.

Note: The January 1, 1968 date for meeting the 12 months' laboratory direction requirement in paragraph (b)(5) of this section may be extended 1 year for each year of full-time laboratory experience obtained before January 1, 1958 required by State law for a laboratory director license. An exception to the July 1, 1971 qualifying date in paragraph (b)(5) of this section was made provided that the individual requested qualification approval by October 21, 1975 and had been employed in a laboratory for at least 3 years of the 5 years preceding the date of submission of his qualifications.

D6004

§493.1407 Standard; Laboratory director responsibilities.

The laboratory director is responsible for the overall operation and administration of the laboratory, including the employment of personnel who are competent to perform test procedures, and record and report test results promptly, accurate, and proficiently and for assuring compliance with the applicable regulations.

Interpretative Guidelines §493.1407

If the laboratory has more than one person qualifying as director, the laboratory is required to designate one individual who has ultimate responsibility for overall operation and administration of the laboratory.

The requirement that a laboratory must be under the direction of a qualified person is not automatically met simply because the director meets the education and experience requirements. It must be demonstrated that the individual is, in fact, providing effective direction over the operation of the laboratory.

In determining whether the director responsibilities are met, consider deficiencies found in other conditions, e.g., facility administration, general laboratory systems, preanalytic systems, analytic systems, postanalytic systems, and proficiency testing.

a) The laboratory director, if qualified, may perform the duties of the technical consultant, clinical consultant, and testing personnel, or delegate these responsibilities to personnel meeting the qualifications of §§493.1409, 493.1415, and 493.1421, respectively.

Interpretative Guidelines §493.1407(a)

If the laboratory director is not qualified as a technical consultant or clinical consultant, he or she must employ individuals meeting the appropriate qualifications.

(b) If the laboratory director reapportions performance of his or her responsibilities, he or she remains responsible for ensuring that all duties are properly performed.

D6005

§493.1407 Standard; Laboratory director responsibilities.

(c) The laboratory director must be accessible to the laboratory to provide onsite, telephone or electronic consultation as needed.

Interpretative Guidelines §493.1407(c)

If the director cannot practically provide personal, onsite supervision it must be demonstrated that the director:

- *Provides direction and consultation by telephone, as necessary; or*
- *Delegates to qualified personnel specific responsibilities as provided in the regulations.*

The laboratory director may reapportion to a technical consultant, in writing, the responsibilities in: §§493.1407(e)(3), (4), (5), (6), (7), (11), (12), and (13).

The laboratory director may reapportion to a clinical consultant, in writing, the responsibilities in: §§493.1407(e)(8) and (9).

D6006

§493.1407 Standard; Laboratory director responsibilities.

(d) Each individual may direct no more than five laboratories.

Interpretative Guidelines §493.1407(d)

An individual may serve as a director of 5 certified laboratories. An individual may serve as a technical consultant or clinical consultant for any number of laboratories.

D6007

§493.1407 Standard; Laboratory director responsibilities.

(e) The laboratory director must--

(e)(1) Ensure that testing systems developed and used for each of the tests performed in the laboratory provide quality laboratory services for all aspects of test performance, which includes the preanalytic, analytic, and postanalytic phases of testing;

D6010

§493.1407 Standard; Laboratory director responsibilities.

(e)(2) Ensure that the physical plant and environmental conditions of the laboratory are appropriate for the testing performed and

Interpretative Guidelines §493.1407(e)(2)

OSHA/EPA issues cannot be cited using these requirements. If immediate jeopardy exists, the director should be informed immediately.

If you observe or obtain information regarding potential safety violations not applicable under CLIA, notify the appropriate State or local authority. Consult with the Regional Office (RO) for notification to other Federal agencies such as the Occupational Safety

and Health Administration (OSHA) www.osha.gov, Environmental Protection Agency (EPA) www.epa.gov, or Nuclear Regulatory Commission (NRC). The appropriate Federal, State or local authority, if warranted, will investigate and, if necessary, conduct an on-site visit.

D6011

§493.1407 Standard; Laboratory director responsibilities.

provide a safe environment in which employees are protected from physical, chemical, and biological hazards;

D6012

§493.1407 Standard; Laboratory director responsibilities.

(e)(3) Ensure that--

(e)(3)(i) The test methodologies selected have the capability of providing the quality of results required for patient care;

D6013

§493.1407 Standard; Laboratory director responsibilities.

(e)(3)(ii) Verification procedures used are adequate to determine the accuracy, precision, and other pertinent performance characteristics of the method; and

D6014

§493.1407 Standard; Laboratory director responsibilities.

(e)(3)(iii) Laboratory personnel are performing the test methods as required for accurate and reliable results;

D6015

§493.1407 Standard; Laboratory director responsibilities.

(e)(4) Ensure that the laboratory is enrolled in an HHS approved proficiency testing program for the testing performed and that--

D6016

§493.1407 Standard; Laboratory director responsibilities.

(e)(4)(i) The proficiency testing samples are tested as required under subpart H of this part;

D6017

§493.1407 Standard; Laboratory director responsibilities.

(e)(4)(ii) The results are returned within the timeframes established by the proficiency testing program;

D6018

§493.1407 Standard; Laboratory director responsibilities.

(e)(4)(iii) All proficiency testing reports received are reviewed by the appropriate staff to evaluate the laboratory's performance and to identify any problems that require corrective action; and

D6019

§493.1407 Standard; Laboratory director responsibilities.

(e)(4)(iv) An approved corrective action plan is followed when any proficiency testing results are found to be unacceptable or unsatisfactory;

D6020

§493.1407 Standard; Laboratory director responsibilities.

(e)(5) Ensure that the quality control

D6021

§493.1407 Standard; Laboratory director responsibilities.

and quality assessment programs are established and maintained to assure the quality of laboratory services provided and

D6022

§493.1407 Standard; Laboratory director responsibilities.

to identify failures in quality as they occur;

D6023

§493.1407 Standard; Laboratory director responsibilities.

(e)(6) Ensure the establishment and maintenance of acceptable levels of analytical performance for each test system;

D6024

§493.1407 Standard; Laboratory director responsibilities.

(e)(7) Ensure that all necessary remedial actions are taken and documented whenever significant deviations from the laboratory's established performance specifications are identified, and

D6025

§493.1407 Standard; Laboratory director responsibilities.

that patient test results are reported only when the system is functioning properly;

D6026

§493.1407 Standard; Laboratory director responsibilities.

(e)(8) Ensure that reports of test results include pertinent information required for interpretation;

D6027

§493.1407 Standard; Laboratory director responsibilities.

(e)(9) Ensure that consultation is available to the laboratory's clients on matters relating to the quality of the test results reported and their interpretation concerning specific patient conditions;

D6028

§493.1407 Standard; Laboratory director responsibilities.

(e)(10) Employ a sufficient number of laboratory personnel with the appropriate education and either experience or training to provide appropriate consultation, properly supervise and accurately perform tests and report test results in accordance with the personnel responsibilities described in this subpart;

D6029

§493.1407 Standard; Laboratory director responsibilities.

(e)(11) Ensure that prior to testing patients' specimens, all personnel have the appropriate education and experience, receive the appropriate training for the type and complexity of the services offered, and have demonstrated that they can perform all testing operations reliably to provide and report accurate results;

D6030

§493.1407 Standard; Laboratory director responsibilities.

(e)(12) Ensure that policies and procedures are established for monitoring individuals who conduct preanalytical, analytical, and postanalytical phases of testing to assure that they are competent and maintain their competency to process specimens, perform test procedures and report test results promptly and proficiently, and whenever necessary, identify needs for remedial training or continuing education to improve skills;

D6031

§493.1407 Standard; Laboratory director responsibilities.

(e)(13) Ensure that an approved procedure manual is available to all personnel responsible for any aspect of the testing process; and

D6032

§493.1407 Standard; Laboratory director responsibilities.

(e)(14) Specify, in writing, the responsibilities and duties of each consultant and each person, engaged in the performance of the preanalytic, analytic, and postanalytic phases of testing, that identifies which examinations and procedures each individual is authorized to perform, whether supervision is required for specimen processing, test performance or results reporting, and whether consultant or director review is required prior to reporting patient test results.

Interpretative Guidelines §493.1407(e)(14)

The director must assign, in writing, the duties/responsibilities to each person involved in all phases of the testing process. The list of assigned duties must be current.

D6033

§493.1409 Condition: Laboratories performing moderate complexity testing; technical consultant.

The laboratory must have a technical consultant who meets the qualification requirements of §493.1411 of this subpart and provides technical oversight in accordance with §493.1413 of this subpart.

Interpretative Guidelines §493.1409

The Condition of technical consultant is not met when the technical consultant:

- *Position is not filled;*
- *Is not qualified; or*
- *Does not fulfill the technical consultant's responsibilities.*

D6034

§493.1411 Standard; Technical consultant qualifications.

The laboratory must employ one or more individuals who are qualified by education and either training or experience to provide technical consultation for each of the specialties and subspecialties of service in which the laboratory performs moderate complexity tests or procedures. The director of a laboratory performing moderate complexity testing may function as the technical consultant provided he or she meets the qualifications specified in this section.

Interpretative Guidelines §493.1411

The type of experience required under this regulation is clinical in nature. This means, examination and test performance on human specimens for purposes of obtaining information for the diagnosis, treatment, and monitoring of patients, or for providing information to others who will do the diagnosing and treating of the patient's condition. Patient or medically-oriented experience, which is defined as the ordering of tests and

interpreting and applying the results of these tests in diagnosing and treating a patient's illness is unacceptable to meet the requirement for laboratory training or experience.

The term "laboratory training or experience" means that the individual qualifying has the training and experience in the specialties and subspecialties in which the individual is providing technical consultation.

Technical consultants should have documentation of hands-on testing experience. This documentation may consist of, but is not limited to, the individual's initials on worksheets or work cards, attestation of the laboratory director to the experience the individual has, or formal laboratory rotation through a medical residency program or laboratory internship program.

Teaching experience directly related to a medical technology program, clinical laboratory sciences program, or a clinical laboratory section of a residency program is considered acceptable experience. Research experience is also acceptable experience if it is obtained while performing tests on human specimens.

D6035

§493.1411 Standard; Technical consultant qualifications.

(a) The technical consultant must possess a current license issued by the State in which the laboratory is located, if such licensing is required.

(b) The technical consultant must--

(b)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(b)(1)(ii) Be certified in anatomic or clinical pathology, or both, by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

§493.1411(b)(1)(ii) Guidelines:

Qualifications that are equivalent for certification include board eligibility, i.e., the individual meets all education, training, or experience requirements to take the examination, but has not actually taken and successfully completed the examination. An individual who wishes to qualify as a technical consultant must supply evidence of this eligibility status. The designated boards, upon request, will send a letter to the individual confirming his/her eligibility status. Note that some boards set time restrictions for taking the examination. For purposes of the regulations, the individual must meet the education, training or experience required by the board to be eligible to take the examination and must have confirmation of eligibility status.

(b)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(b)(2)(ii) Have at least one year of laboratory training or experience, or both in non-waived testing, in the designated specialty or subspecialty areas of service for which the technical consultant is responsible (for example, physicians certified either in hematology or hematology and medical oncology by the American Board of Internal Medicine are qualified to serve as the technical consultant in hematology); or

(b)(3)(i) Hold an earned doctoral or master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(b)(3)(ii) Have at least one year of laboratory training or experience, or both in non-waived testing, in the designated specialty or subspecialty areas of service for which the technical consultant is responsible; or

(b)(4)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and
(b)(4)(ii) Have at least 2 years of laboratory training or experience, or both in non-waived testing, in the designated specialty or subspecialty areas of service for which the technical consultant is responsible.

Note: The technical consultant requirements for "laboratory training or experience, or both" in each specialty or subspecialty may be acquired concurrently in more than one of the specialties or subspecialties of service, excluding waived tests. For example, an individual who has a bachelor's degree in biology and additionally has documentation of 2 years of work experience performing tests of moderate complexity in all specialties and subspecialties of service, would be qualified as a technical consultant in a laboratory performing moderate complexity testing in all specialties and subspecialties of service.

Interpretative Guidelines §493.1411(b)(3)-(b)(4)

See §493.2 for the definition of and guidance for accredited institution.

Some examples of how the one-year requirement for training or experience can be met are:

- *Medical technology internship;*
- *1 year experience performing non-waived tests in a particular specialty(ies) or subspecialty(ies); or*
- *Performance of non-waived testing in a particular specialty(ies) or subspecialty(ies) on a part-time basis, equivalent to 2080 hours.*

NOTE: §493.1411(b)(4) requires 2 years of laboratory training or experience and can be met by any combination equivalent to 2 years of laboratory training or experience.

D6036

§493.1413 Standard; Technical consultant responsibilities.

The technical consultant is responsible for the technical and scientific oversight of the laboratory.

Interpretative Guidelines §493.1413

In a specialty in which neither the director nor testing personnel can qualify to provide technical consultation, the laboratory may engage the services of a qualified person either on a part-time or full-time basis for this service. Under these circumstances, the qualified person is not required to be on the premises full-time or at all times tests are being performed in his/her specialty(ies). However, the technical consultant must be available to provide consultation and should spend time in the laboratory sufficient to supervise the technical performance of the staff in his/her specialty(ies).

D6037

§493.1413 Standard; Technical consultant responsibilities.

The technical consultant is not required to be onsite at all times testing is performed; however, he or she must be available to the laboratory on an as needed basis to provide consultation, as specified in paragraph (a) of this section.

D6038

§493.1413 Standard; Technical consultant responsibilities.

(a) The technical consultant must be accessible to the laboratory to provide on-site, telephone, or electronic consultation; and

Interpretative Guidelines §493.1413(a)

Since the testing personnel usually will not have experience and training in all specialties, technical consultation is essential in identifying training needs and assuring that each individual performing testing receives regular in-service training and education. There should be documentation, such as a log book or training/discussion reports, to indicate the services provided or activities performed by the technical consultant. These activities should correlate with the responsibilities delegated to the technical consultant by the laboratory director. The technical consultant is responsible for evaluating the capabilities of the technical personnel and advising the director on proper test performance in the specialty.

D6039

§493.1413 Standard; Technical consultant responsibilities.

(b) The technical consultant is responsible for--

(b)(1) Selection of test methodology appropriate for the clinical use of the test results;

D6040

§493.1413 Standard; Technical consultant responsibilities.

(b)(2) Verification of the test procedures performed and the establishment of the laboratory's test performance characteristics, including the precision and accuracy of each test and test system;

D6041

§493.1413 Standard; Technical consultant responsibilities.

(b)(3) Enrollment and participation in an HHS approved proficiency testing program commensurate with the services offered;

D6042

§493.1413 Standard; Technical consultant responsibilities.

(b)(4) Establishing a quality control program appropriate for the testing performed and establishing the parameters for acceptable levels of analytic performance and ensuring that these levels are maintained throughout the entire testing process from the initial receipt of the specimen, through sample analysis and reporting of test results;

D6043

§493.1413 Standard; Technical consultant responsibilities.

(b)(5) Resolving technical problems and ensuring that remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications;

D6044

§493.1413 Standard; Technical consultant responsibilities.

(b)(6) Ensuring that patient test results are not reported until all corrective actions have been taken and the test system is functioning properly;

D6045

§493.1413 Standard; Technical consultant responsibilities.

(b)(7) Identifying training needs and assuring that each individual performing tests receives regular in-service training and education appropriate for the type and complexity of the laboratory services performed;

Interpretative Guidelines §493.1413(b)(7)

In some instances, in-service training may be specifically related to an instrument or test, or may be very general in nature. The laboratory may establish its own format, content, and schedule or provide training on an as-needed basis. This is acceptable provided the laboratory does not have deficiencies related to test performance.

D6046

§493.1413 Standard; Technical consultant responsibilities.

(b)(8) Evaluating the competency of all testing personnel and assuring that the staff maintain their competency to perform test procedures and report test results promptly, accurately and proficiently. The procedures for evaluation of the competency of the staff must include, but are not limited to--

Probes §493.1413(b)(8)

What mechanism is used to ensure that testing personnel are following the laboratory's policies and procedures?

Evaluations of technical and clinical consultants' performance is located at §493.1235 - Personnel Competency Assessment Policies and §§493.1239(a)-(b), General Laboratory Systems Assessment.

D6047

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(i) Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing and testing;

D6048

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(ii) Monitoring the recording and reporting of test results;

D6049

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(iii) Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records;

D6050

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(iv) Direct observation of performance of instrument maintenance and function checks;

D6051

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(v) Assessment of test performance through testing previously analyzed specimens, internal blind testing samples or external proficiency testing samples; and

D6052

§493.1413 Standard; Technical consultant responsibilities.

(b)(8)(vi) Assessment of problem solving skills; and

D6053

§493.1413 Standard; Technical consultant responsibilities.

(b)(9) Evaluating and documenting the performance of individuals responsible for moderate complexity testing at least semiannually during the first year the individual tests patient specimens.

D6054

§493.1413 Standard; Technical consultant responsibilities.

Thereafter, evaluations must be performed at least annually

D6055

§493.1413 Standard; Technical consultant responsibilities.

unless test methodology or instrumentation changes, in which case, prior to reporting patient test results, the individual's performance must be reevaluated to include the use of the new test methodology or instrumentation.

D6056

§493.1415 Condition: Laboratories performing moderate complexity testing; clinical consultant.

The laboratory must have a clinical consultant who meets the qualification requirements of §493.1417 of this part and provides clinical consultation in accordance with §493.1419 of this part.

Interpretative Guidelines §493.1415

The Condition of clinical consultant is not met when the clinical consultant:

- *Position is not filled;*
- *Is not qualified; or*
- *Does not fulfill the clinical consultant's responsibilities.*

D6057

§493.1417 Standard; Clinical consultant qualifications.

The clinical consultant must be qualified to consult with and render opinions to the laboratory's clients concerning the diagnosis, treatment and management of patient care. The clinical consultant must--

- (a) Be qualified as a laboratory director under §493.1405(b)(1), (2), or (3)(i); or
- (b) Be a doctor of medicine, doctor of osteopathy or doctor of podiatric medicine and possess a license to practice medicine, osteopathy or podiatry in the State in which the laboratory is located.

D6058

§493.1419 Standard; Clinical consultant responsibilities.

The clinical consultant provides consultation regarding the appropriateness of the testing ordered and interpretation of test results.

D6059

§493.1419 Standard; Clinical consultant responsibilities.

The clinical consultant must--

- (a) Be available to provide clinical consultation to the laboratory's clients;

D6060

§493.1419 Standard; Clinical consultant responsibilities.

- (b) Be available to assist the laboratory's clients in ensuring that appropriate tests are ordered to meet the clinical expectations;

D6061

§493.1419 Standard; Clinical consultant responsibilities.

(c) Ensure that reports of test results include pertinent information required for specific patient interpretation; and

Probes §493.1419(c)

Has the clinical consultant reviewed the reports to ensure that test results include patient information required for specific patient interpretations?

D6062

§493.1419 Standard; Clinical consultant responsibilities.

(d) Ensure that consultation is available and communicated to the laboratory's clients on matters related to the quality of the test results reported and their interpretation concerning specific patient conditions.

D6063

§493.1421 Condition: Laboratories performing moderate complexity testing; testing personnel.

The laboratory must have a sufficient number of individuals who meet the qualification requirements of §493.1423, to perform the functions specified in §493.1425 for the volume and complexity of tests performed.

Interpretative Guidelines §493.1421

The criteria used to determine the adequacy of the testing personnel involves evaluating testing personnel responsibilities, and ensuring that these responsibilities are specified in writing by the director, and that the responsibilities are appropriate to ensure compliance with the requirements concerning reporting and recordkeeping, quality control monitoring, quality assurance activities and proficiency testing participation. Cite this deficiency only when compliance problems are found in these areas that can be directly related to insufficient numbers of testing personnel. (Use D6028, which relates the finding of insufficient personnel to director responsibilities.)

D6064

§493.1423 Standard; Testing personnel qualifications.

Each individual performing moderate complexity testing must--

(a) Possess a current license issued by the State in which the laboratory is located, if such licensing is required; and

Interpretative Guidelines §493.1423

The laboratory director is responsible for ensuring the testing personnel have the appropriate education and experience, and receive the appropriate training for the type and complexity of testing performed. The experience required is clinical in nature. This means, examination of and test performance on human specimens for purposes of obtaining information for the diagnosis, treatment, and monitoring of patients, or for providing information to others who will do the diagnosing and treating of the patient's condition. (Use D6029).

Each individual must have documentation of training applicable to the types and complexity of testing performed. This training should be such that the individual can

demonstrate that he/she has the skills required for proper performance of preanalytic, analytic, and postanalytic phases of testing. For example, if the individual performs a rapid Strep test, he/she should be able to demonstrate the skills for:

- Proper specimen handling prior to testing, e.g., assuring the specimen is properly labeled and received and tested within appropriate timeframes, the swab is received at the proper temperature, and the ampule on the swab containing transport media is broken;
- Proper test performance according to the laboratory's policies and manufacturer's instructions, e.g., using reagents that are not outdated, are at the proper temperature, and of the same lot number, accurate timing of all steps in the procedure, proper performance of quality control procedures; and
- Proper reporting of patient test results in accordance with the laboratory's policies, e.g., notifying the person authorized to receive test results of a positive result, not reporting the test result if quality control fails.

Training may include, but is not limited to, attendance at:

- Seminars given by experts in the field, e.g., a lecture about antibiotic resistance given by the infection control officer of a local hospital;
- On-site or off-site instrument trainings given by a manufacturer, e.g., a week-long training course given at the manufacturer's headquarters, or training by a manufacturer's technical representative on an instrument purchased by a laboratory;
- Technical training sessions, workshops, or conferences given by a professional laboratory organization, e.g., CAP, ASMT, AACC, and ASCT;
- Technical education classes or specialty courses that include hands-on test performance, e.g., parasitology, bacteriology, cytology, given by CDC, a State Health Department, or professional laboratory organizations;
- A formal laboratory training program; or
- Inservices offered by a local hospital laboratory staff, pathologist, or medical technologist to a physician's office personnel.

Documentation may consist of, but is not limited to, letters from training programs or employers, attestation statements by the laboratory director, a log sheet initialed by the attendees indicating attendance at a training session/in-service, certificates from organizations providing the training session, workshop, conference, specialty course.

D6065

§493.1423 Standard; Testing personnel qualifications.

(b) Meet one of the following requirements:

(b)(1) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located or have earned a doctoral, master's, or bachelor's degree in a chemical, physical, biological or clinical laboratory science, or medical technology from an accredited institution; or

Interpretative Guidelines §493.1423(b)(1)

See §493.2 for the definition of and guidance for accredited institution.

(b)(2) Have earned an associate degree in a chemical, physical or biological science or medical laboratory technology from an accredited institution; or

(b)(3) Be a high school graduate or equivalent and have successfully completed an official military medical laboratory procedures course of at least 50 weeks duration and have held the military enlisted occupational specialty of Medical Laboratory Specialist (Laboratory

Technician); or

Interpretative Guidelines §493.1423(b)(3)

Equate similar military courses with different titles. Evaluate the course length and content to assure that it provides effective training for testing personnel. Refer to A Guide to the Evaluation of Educational Experience in the Armed Services, American Council on Education, Washington, D.C.

(b)(4)(i) Have earned a high school diploma or equivalent; and

Interpretative Guidelines §493.1423(b)(4)

Personnel qualifying under this requirement must have a high school diploma or GED.

Probes §1493.1423(b)(4)

How does the laboratory assure that personnel receiving orientation and training have the necessary skills for properly performing assigned responsibilities?

D6066

§493.1423 Standard; Testing personnel qualifications.

(b)(4)(ii) Have documentation of training appropriate for the testing performed prior to analyzing patient specimens.

D6067

§493.1423 Standard; Testing personnel qualifications.

Such training must ensure that the individual has--

- (b)(4)(ii)(A) The skills required for proper specimen collection, including patient preparation, if applicable, labeling, handling, preservation or fixation, processing or preparation, transportation and storage of specimens;**
- (b)(4)(ii)(B) The skills required for implementing all standard laboratory procedures;**
- (b)(4)(ii)(C) The skills required for performing each test method and for proper instrument use;**
- (b)(4)(ii)(D) The skills required for performing preventive maintenance, troubleshooting and calibration procedures related to each test performed;**
- (b)(4)(ii)(E) A working knowledge of reagent stability and storage;**
- (b)(4)(ii)(F) The skills required to implement the quality control policies and procedures of the laboratory;**
- (b)(4)(ii)(G) An awareness of the factors that influence test results; and**
- (b)(4)(ii)(H) The skills required to assess and verify the validity of patient test results through the evaluation of quality control sample values prior to reporting patient test results.**

D6068

§493.1425 Standard; Testing personnel responsibilities.

The testing personnel are responsible for specimen processing, test performance, and for reporting test results.

D6069

§493.1425 Standard; Testing personnel responsibilities.

(a) Each individual performs only those moderate complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities.

D6070

§493.1425 Standard; Testing personnel responsibilities.

(b) Each individual performing moderate complexity testing must--

(b)(1) Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting and maintaining records of patient test results;

D6071

§493.1425 Standard; Testing personnel responsibilities.

(b)(2) Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient samples;

D6072

§493.1425 Standard; Testing personnel responsibilities.

(b)(3) Adhere to the laboratory's quality control policies, document all quality control activities, instrument and procedural calibrations and maintenance performed;

D6073

§493.1425 Standard; Testing personnel responsibilities.

(b)(4) Follow the laboratory's established corrective action policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance;

D6074

§493.1425 Standard; Testing personnel responsibilities.

(b)(5) Be capable of identifying problems that may adversely affect test performance or reporting of test results and either must correct the problems or immediately notify the technical consultant, clinical consultant or director; and

Interpretative Guidelines §493.1425(b)(5)

If, during the survey, testing personnel demonstrate an inability to identify a problem that adversely affects a patient test result, cite D6029 under director responsibilities.

Some examples of problems that may adversely affect patient test results may include, but are not limited to:

- *A pleural fluid that is mislabeled and, therefore, is processed as a urine culture;*

- *Performing a potassium on a hemolyzed sample; or*
- *Tests are incubated at 37°C when the manufacturer's instructions require 25°C incubation.*

D6075

§493.1425 Standard; Testing personnel responsibilities.

(b)(6) Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications.

D6076

Laboratories Performing High Complexity Testing

§493.1441 Condition: Laboratories performing high complexity testing; laboratory director.

The laboratory must have a director who meets the qualification requirements of §493.1443 of this subpart and provides overall management and direction in accordance with §493.1445 of this subpart.

Interpretative Guidelines §493.1441

The Condition of laboratory director is not met when the laboratory director:

- *Position is not filled;*
- *Is not qualified; or*
- *Does not fulfill the laboratory director responsibilities.*

D6077

§493.1443 Standard; Laboratory director qualifications.

The laboratory director must be qualified to manage and direct the laboratory personnel and performance of high complexity tests and must be eligible to be an operator of a laboratory within the requirements of subpart R.

Interpretative Guidelines §493.1443

Section 353(i)(3) of the PHS Act states "No person who has owned or operated a laboratory which has had its certificate revoked may, within 2 years of the revocation of the certificate, own or operate a laboratory for which a certificate has been issued under this section."

The term "State" as used in this provision, includes the District of Columbia, the Commonwealth of Puerto Rico, the Commonwealth of Northern Mariana Islands, the Virgin Islands, Guam and American Samoa.

D6078

§493.1443 Standard; Laboratory director qualifications.

(a) The laboratory director must possess a current license as a laboratory director issued by the State in which the laboratory is located, if such licensing is required; and

(b) The laboratory director must--

(b)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(b)(1)(ii) Be certified in anatomic or clinical pathology, or both, by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1443(b)(1)(ii)

Qualifications that are equivalent for certification include board eligibility, i.e., the individual meets all education, training, or experience requirements to take the examination, but has not actually taken and successfully completed the examination. An individual who wishes to qualify as a director must supply evidence of this eligibility status. The designated boards, upon request, will send a letter to the individual confirming his/her eligibility status. Note that some boards set time restrictions for taking the examination. For purposes of the regulations, the individual must meet the education, training, or experience as required by the board to be eligible to take the examination and must have confirmation of eligibility status.

(b)(2) Be a doctor of medicine, a doctor of osteopathy or doctor of podiatric medicine licensed to practice medicine, osteopathy or podiatry in the State in which the laboratory is located; and

(b)(2)(i) Have at least one year of laboratory training during medical residency (for example, physicians certified either in hematology or hematology and medical oncology by the American Board of Internal Medicine); or

Interpretative Guidelines §493.1443(b)(2)(i)

The residency program should provide the director the knowledge in principles and theories of laboratory practice including: quality control and quality assessment, proficiency testing, the phase of the total process (i.e., preanalytic, analytic and postanalytic), as well as, general laboratory systems, facility administration, and development and implementation of personnel policy and procedure manuals. This training should also include hands-on laboratory testing.

(b)(2)(ii) Have at least 2 years of experience directing or supervising high complexity testing; or

Interpretative Guidelines §493.1443(b)(2)(ii)

The type of experience required under this regulation is clinical in nature. This means directing or supervising personnel who examine and perform tests on human specimens for the purpose of providing information that is used in diagnosing, treating, and monitoring a patient's condition. This experience may include the laboratory director personally examining and performing tests on patient specimens. Patient or medically-oriented experience, which is defined as the ordering of tests and interpreting and applying the results of these tests in diagnosing and treating a patient's illness is unacceptable to meet the requirement for laboratory training or experience.

The laboratory director should have documentation, e.g., signed procedure manuals, test reports, worksheets and workcards, that indicates the director assumes the responsibilities in §493.1445.

Teaching experience directly related to a medical technology program, clinical laboratory sciences program, or a clinical laboratory section of a residency program is considered acceptable experience. Research experience is also acceptable experience if it is obtained while performing tests on human specimens.

- (b)(3) Hold an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution and--**
(b)(3)(i) Be certified and continue to be certified by a board approved by HHS; or

Interpretative Guidelines §493.1443(b)(3)

See §493.2 for the definition of and guidance for accredited institution.

To qualify as a laboratory director of high complexity testing on or after February 24, 2003, individuals possessing a Ph.D. or Dr.P.H. must be board certified by an approved board.

“Certified” means the individual has completed all the designated board’s requirements, including the examination.

Currently approved boards are:

*American Board of Bioanalysis (ABB),
American Board of Clinical Chemistry (ABCC),
American Board of Forensic Toxicology (ABFT),
American Board of Histocompatibility and Immunogenetics (ABHI),
American Board of Medical Genetics (ABMG),
American Board of Medical Laboratory Immunology (ABMLI),
American Board of Medical Microbiology (ABMM),
National Registry for Clinical Chemists (NRCC), or other board deemed comparable by HHS. NOTE: ABFT and NRCC also certify non-doctorial individuals; however, the director of high-complexity testing must have a doctoral degree.*

An acceptable doctoral degree is a Doctor of Philosophy – Ph.D., Doctor of Science – D.Sc. If acceptable to the board, a Doctor of Dental Surgery – D.D.S., Doctor of Veterinary Medicine – D.V.M., Doctor of Public Health – Dr.P.H.

Laboratory testing of non-human specimens is not acceptable experience, e.g., environmental, animal testing.

- (b)(3)(ii) Before February 24, 2003, must have served or be serving as director of a laboratory performing high complexity testing and must have at least--**
(b)(3)(ii)(A) Two years of laboratory training or experience, or both; and
(b)(3)(ii)(B) Two years of laboratory experience directing or supervising high complexity testing.
(b)(4) Be serving as a laboratory director and must have previously qualified or could have qualified as a laboratory director under regulations at 42 CFR 493.1415, published March 14, 1990 at 55 FR 9538, on or before February 28, 1992; or

Interpretative Guidelines §493.1443(b)(4)

An individual is qualified as a laboratory director if he or she was serving as a laboratory director on or before February 28, 1992. After February 28, 1992, individuals must meet the requirements at §493.1443(b)(1)-(3) to qualify as a laboratory director for high complexity.

In accordance with the regulations, the requirements listed below may be used only for individuals meeting these qualifications and functioning in the position as of February 28, 1992.

The requirements for a laboratory director under 42 CFR 493.1415, published March 14, 1990 (55 FR 9538) are as follows:

(a) *The laboratory director must possess a current license as a laboratory director issued by the State, if such licensing exists; and*

(b) *The laboratory director must:*

(b)(1) *Be a physician certified in anatomical or clinical pathology (or both) by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification;*

(b)(2) *Be a physician who: (b)(2)(i) is certified by the American Board of Pathology or the American Osteopathic Board of Pathology in at least one of the laboratory specialties, or (b)(2)(ii) is certified by the American Board of Medical Microbiology, the American Board of Clinical Chemistry, the American Board of Bioanalysis, or other national accrediting board in one of the laboratory specialties, or (b)(2)(iii) is certified by the American Society of Cytology to practice cytopathology or possesses qualifications that are equivalent to those required for such certification, or (b)(2)(iv) subsequent to graduation, has had 4 or more years of full-time general laboratory training and experience of which at least 2 years were spent acquiring proficiency in one of the laboratory specialties;*

(b)(3) *For the subspecialty of oral pathology only, be certified by the American Board of Oral Pathology, American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for certification;*

(b)(4) *Hold an earned doctoral degree from an accredited institution with a chemical, physical, or biological science as a major subject and (b)(4)(i) is certified by the American Board of Medical Microbiology, the American Board of Clinical Chemistry, the American Board of Bioanalysis, or other national accrediting board acceptable to HHS in one of the laboratory specialties, or (b)(4)(ii) subsequent to graduation has had 4 or more years of full time general laboratory training and experience of which at least 2 years were spent acquiring proficiency in one of the laboratory specialties;*

(b)(5) *With respect to individuals first qualifying before July 1, 1971, have been responsible for the direction of a laboratory for 12 months between July 1, 1961, and January 1, 1968, and in addition, either:*

(b)(5)(i) *Was a physician and subsequent to graduation had at least 4 years of pertinent full-time laboratory experience;*

(b)(5)(ii) *Held a master's degree from an accredited institution with a chemical, physical, or biological science as a major subject and subsequent to graduation had at least 4 years of pertinent full-time laboratory experience;*

(b)(5)(iii) *Held a bachelor's degree from an accredited institution with a chemical, physical, or biological science as a major subject and subsequent to graduation had at least 6 years of pertinent full-time laboratory experience; or*

(b)(5)(iv) *Achieved a satisfactory grade through an examination conducted by or under the sponsorship of the U.S. Public Health Service on or before July 1, 1970; or*

(b)(6) *Qualify under State law to direct the laboratory in the State in which the laboratory is located.*

NOTE: *The January 1, 1988, date for meeting the 12 months' laboratory direction requirement in paragraph (b)(5) of this section may be extended 1 year for each year of full-time laboratory experience obtained before January 1, 1968, required by State law for a laboratory director license. An exception to the July 1, 1971, qualifying date in paragraph (b)(5) of this section was made provided that the individual requested qualification approval by October 21, 1975, and had been employed in a laboratory for at least 3 years of the 5 years preceding the date of submission of his qualifications.*

(b)(5) On or before February 28, 1992, be qualified under State law to direct a laboratory in the State in which the laboratory is located; or

Interpretative Guidelines §493.1443(b)(5)

Those individuals qualified after February 28, 1992, as directors solely under State law, will not meet this requirement.

(b)(6) For the subspecialty of oral pathology, be certified by the American Board of Oral Pathology, American Board of Pathology, the American Osteopathic Board of Pathology, or possess qualifications that are equivalent to those required for certification.

D6079

§493.1445 Standard; Laboratory director responsibilities.

The laboratory director is responsible for the overall operation and administration of the laboratory, including the employment of personnel who are competent to perform test procedures, record and report test results promptly, accurately and proficiently, and for assuring compliance with the applicable regulations.

Interpretative Guidelines §493.1445

The requirement that a laboratory must be under the direction of a qualified person is not automatically met simply because the director meets the education and experience requirements. It must be demonstrated that the individual is, in fact, providing effective direction over the operation of the laboratory.

In determining whether the director responsibilities are met, consider deficiencies found in other conditions, e.g., facility administration, general laboratory systems, preanalytic systems, analytic systems, postanalytic systems, and proficiency testing.

If the laboratory has more than one person qualifying as a director, one individual must be designated as accepting ultimate responsibility for the overall operation and administration of the laboratory.

(a) The laboratory director, if qualified, may perform the duties of the technical supervisor, clinical consultant, general supervisor, and testing personnel, or delegate these responsibilities to personnel meeting the qualifications under §§493.1447, 493.1453, 493.1459, and 493.1487, respectively.

Interpretative Guidelines §493.1445(a)

An individual qualified as laboratory director under §493.1443 may not qualify as technical supervisor in a particular specialty or subspecialty unless he or she has the required training or experience. If the director of high complexity testing is not qualified to perform the duties of the technical supervisor or clinical consultant, he or she must employ individual(s) meeting the respective qualifications.

(b) If the laboratory director reappoints performance of his or her responsibilities, he or she remains responsible for ensuring that all duties are properly performed.

D6080

§493.1445 Standard; Laboratory director responsibilities.

(c) The laboratory director must be accessible to the laboratory to provide onsite, telephone or electronic consultation as needed.

D6081

§493.1445 Standard; Laboratory director responsibilities.

(d) Each individual may direct no more than five laboratories.

Interpretative Guidelines §493.1445(d)

An individual may serve as a director of 5 nonwaived certified laboratories. However, an individual may serve as technical consultant, clinical consultant or technical supervisor for any number of laboratories.

D6082

§493.1445 Standard; Laboratory director responsibilities.

(e) The laboratory director must--

(e)(1) Ensure that testing systems developed and used for each of the tests performed in the laboratory provide quality laboratory services for all aspects of test performance, which includes the preanalytic, analytic, and postanalytic phases of testing;

§493.1445(e) Guidelines:

If the director cannot practically provide personal, on-site supervision, it must be demonstrated that the director:

- *Provides direction and consultation electronically or by telephone, as necessary; or*
- *Delegates to qualified personnel specific responsibilities as provided in the regulations.*

The laboratory director may reappportion to a technical supervisor, in writing, the responsibilities in: §§493.1445(e)(3), (4), (5), (6), (7), (12), (13), and (14).

The laboratory director may reappportion to a clinical consultant, in writing, the responsibilities in: §§493.1445(e)(8) and (9).

The only responsibilities that may be delegated to the general supervisor are listed at §§493.1463(b)(1)-(4).

D6083

§493.1445 Standard; Laboratory director responsibilities.

(e)(2) Ensure that the physical plant and environmental conditions of the laboratory are appropriate for the testing performed and

D6084

§493.1445 Standard; Laboratory director responsibilities.

and provide a safe environment in which employees are protected from physical, chemical, and biological hazards;

Interpretative Guidelines §493.1445(e)(2)

OSHA/EPA issues cannot be cited using these requirements. If immediate jeopardy exists, inform the director immediately.

If you observe or obtain information regarding potential safety violations not applicable under CLIA, notify the appropriate State or local authority. Consult with the Regional Office (RO) for notification to other Federal agencies such as the Occupational Safety

and Health Administration (OSHA) www.osha.gov, Environmental Protection Agency (EPA) www.epa.gov, or Nuclear Regulatory Commission (NRC). The appropriate Federal, State or local authority, if warranted, will investigate and, if necessary, conduct an on-site visit.

D6085

§493.1445 Standard; Laboratory director responsibilities.

(e)(3) Ensure that--

(e)(3)(i) The test methodologies selected have the capability of providing the quality of results required for patient care;

D6086

§493.1445 Standard; Laboratory director responsibilities.

(e)(3)(ii) Verification procedures used are adequate to determine the accuracy, precision, and other pertinent performance characteristics of the method; and

D6087

§493.1445 Standard; Laboratory director responsibilities.

(e)(3)(iii) Laboratory personnel are performing the test methods as required for accurate and reliable results;

D6088

§493.1445 Standard; Laboratory director responsibilities.

(e)(4) Ensure that the laboratory is enrolled in an HHS-approved proficiency testing program for the testing performed and that--

D6089

§493.1445 Standard; Laboratory director responsibilities.

(e)(4)(i) The proficiency testing samples are tested as required under subpart H of this part;

D6090

§493.1445 Standard; Laboratory director responsibilities.

(e)(4)(ii) The results are returned within the timeframes established by the proficiency testing program;

D6091

§493.1445 Standard; Laboratory director responsibilities.

(e)(4)(iii) All proficiency testing reports received are reviewed by the appropriate staff to evaluate the laboratory's performance and to identify any problems that require corrective action; and

D6092

§493.1445 Standard; Laboratory director responsibilities.

(e)(4)(iv) An approved corrective action plan is followed when any proficiency testing result is found to be unacceptable or unsatisfactory;

D6093

§493.1445 Standard; Laboratory director responsibilities.

(e)(5) Ensure that the quality control and

D6094

§493.1445 Standard; Laboratory director responsibilities.

quality assessment programs are established and maintained to assure the quality of laboratory services provided and to identify failures in quality as they occur;

D6095

§493.1445 Standard; Laboratory director responsibilities.

(e)(6) Ensure the establishment and maintenance of acceptable levels of analytical performance for each test system;

D6096

§493.1445 Standard; Laboratory director responsibilities.

(e)(7) Ensure that all necessary remedial actions are taken and documented whenever significant deviations from the laboratory's established performance characteristics are identified, and

D6097

§493.1445 Standard; Laboratory director responsibilities.

that patient test results are reported only when the system is functioning properly;

D6098

§493.1445 Standard; Laboratory director responsibilities.

(e)(8) Ensure that reports of test results include pertinent information required for interpretation;

D6099

§493.1445 Standard; Laboratory director responsibilities.

(e)(9) Ensure that consultation is available to the laboratory's clients on matters relating to the quality of the test results reported and their interpretation concerning specific patient conditions;

D6100

§493.1445 Standard; Laboratory director responsibilities.

(e)(10) Ensure that a general supervisor provides on-site supervision of high complexity test performance by testing personnel qualified under §493.1489(b)(4);

D6101

§493.1445 Standard; Laboratory director responsibilities.

(e)(11) Employ a sufficient number of laboratory personnel with the appropriate education and either experience or training to provide appropriate consultation, properly supervise and accurately perform tests and report test results in accordance with the personnel responsibilities described in this subpart;

D6102

§493.1445 Standard; Laboratory director responsibilities.

(e)(12) Ensure that prior to testing patients' specimens, all personnel have the appropriate education and experience, receive the appropriate training for the type and complexity of the services offered, and have demonstrated that they can perform all testing operations reliably to provide and report accurate results;

D6103

§493.1445 Standard; Laboratory director responsibilities.

(e)(13) Ensure that policies and procedures are established for monitoring individuals who conduct preanalytical, analytical, and postanalytical phases of testing to assure that they are competent and maintain their competency to process specimens, perform test procedures and report test results promptly and proficiently, and whenever necessary, identify needs for remedial training or continuing education to improve skills;

D6106

§493.1445 Standard; Laboratory director responsibilities.

(e)(14) Ensure that an approved procedure manual is available to all personnel responsible for any aspect of the testing process; and

D6107

§493.1445 Standard; Laboratory director responsibilities.

(e)(15) Specify, in writing, the responsibilities and duties of each consultant and each supervisor, as well as each person engaged in the performance of the preanalytic, analytic, and postanalytic phases of testing, that identifies which examinations and procedures each individual is authorized to perform, whether supervision is required for specimen processing, test performance or result reporting and whether supervisory or director review is required prior to reporting patient test results.

Interpretative Guidelines §493.1445(e)(15)

The director must assign, in writing, the duties/responsibilities to each person involved in all phases of the testing process. The list of assigned duties must be current.

D6108

§493.1447 Condition: Laboratories performing high complexity testing; technical supervisor.

The laboratory must have a technical supervisor who meets the qualification requirements of §493.1449 of this subpart and provides technical supervision in accordance with §493.1451 of this subpart.

§493.1447 Guidelines:

The Condition of technical supervisor is not met when the technical supervisor:

- *Position is not filled;*
 - *Is not qualified; or*
 - *Does not fulfill the technical supervisor responsibilities.*
-

D6109

§493.1449 Standard; Technical supervisor qualifications.

The laboratory must employ one or more individuals who are qualified by education and either training or experience to provide technical supervision for each of the specialties and subspecialties of service in which the laboratory performs high complexity tests or procedures. The director of a laboratory performing high complexity testing may function as the technical supervisor provided he or she meets the qualifications specified in this section.

Interpretative Guidelines §493.1449

The type of experience required under this regulation is clinical in nature. This means examination and test performance on human specimens for purposes of obtaining information for the diagnosis, treatment, and monitoring of patients, or for providing information to others who will do the diagnosing and treating of the patient's condition. Patient or medically-oriented experience, which is defined as the ordering of tests and interpreting and applying the results of these tests in diagnosing and treating a patient's illness is unacceptable to meet the requirement for laboratory training or experience.

The term "laboratory training or experience" means that the individual qualifying has the training in and the experience with the specialties and subspecialties in which the individual is performing technical supervision. For technical supervisor, the requirement for training or experience can be met through any combination of training and/or experience in high complexity testing. This can be acquired subsequent to, concurrent with, or prior to obtaining academic requirements.

Be flexible in evaluating laboratory training and experience. The specified training or experience may be acquired simultaneously in more than one specialty/subspecialty. Although it is unreasonable in §§493.1449(c)(5) and (j)(5) to expect four full-time years devoted only to high complexity microbiology testing and then four full-time years performing high complexity tests only in hematology, etc., to qualify under each specialty/subspecialty, it is necessary for the individual to have had continuous responsibilities in the specialty for the designated number of years and it would be more than simply performing an occasional test. Technical supervisors should have documentation of hands-on testing experience. This documentation may consist of, but is not limited to, the individual's initials on worksheets or work cards, attestation of the laboratory director to the experience the individual has, or formal laboratory rotation through a medical residency program or laboratory internship program.

Teaching experience directly related to a medical technology program, clinical laboratory sciences program, or a clinical laboratory section of a residency program is considered acceptable experience. Research experience is also acceptable experience if it is obtained while performing tests on human specimens.

A year of laboratory training or experience is equivalent to 2080 hours and could extend over more than one 12 calendar-month period.

D6111

§493.1449 Standard; Technical supervisor qualifications.

- (a) The technical supervisor must possess a current license issued by the State in which the laboratory is located, if such licensing is required; and**
- (b) The laboratory may perform anatomic and clinical laboratory procedures and tests in all specialties and subspecialties of services except histocompatibility and clinical cytogenetics services provided the individual functioning as the technical supervisor--**
 - (b)(1) Is a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and**
 - (b)(2) Is certified in both anatomic and clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or Possesses qualifications that are equivalent to those required for such certification.**

Interpretative Guidelines §493.1449(b)(2)

Qualifications that are equivalent for certification includes board eligibility, i.e., the individual meets all education, training, or experience requirements to take the examination, but has not actually taken and successfully completed the examination. An individual who wishes to qualify as a technical supervisor must supply evidence of this eligibility status. The designated boards, upon request, will send a letter to the individual confirming his/her eligibility status. Note that some boards set time restrictions for taking the examination. For purposes of the regulations, the individual must meet the education, training or experience required by the board to be eligible to take the examination and must have confirmation of eligibility status.

(c) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of bacteriology, the individual functioning as the technical supervisor must--

(c)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(c)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(c)(1)(ii)

See §493.1449(b)(2) Guidelines.

(c)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(c)(2)(ii) Have at least one year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of bacteriology; or

(c)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(c)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(c)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of bacteriology; or

(c)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(c)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of bacteriology; or

(c)(5)(i) Have earned a bachelor's degree in a chemical, physical, or biological science or medical technology from an accredited institution; and

(c)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of bacteriology.

(d) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of mycobacteriology, the individual functioning as the technical supervisor must--

(d)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(d)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(d)(1)(ii)

See §493.1449(b)(2) Guidelines.

(d)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor or podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(d)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycobacteriology; or

(d)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(d)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(d)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycobacteriology; or

(d)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(d)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycobacteriology; or

(d)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and

(d)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycobacteriology.

(e) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of mycology, the individual functioning as the technical supervisor must--

(e)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(e)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(e)(1)(ii)

See §493.1449(b)(2) Guidelines.

(e)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(e)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycology; or

(e)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(e)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(e)(3)(ii) Have at least 1 year of laboratory training or experience, or both in high complexity testing within the speciality of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycology; or

(e)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(e)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycology; or

(e)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and

(e)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of mycology.

(f) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of parasitology, the individual functioning as the technical supervisor must--

(f)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(f)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(f)(1)(ii)

See §493.1449(b)(2) Guidelines.

(f)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(f)(2)(ii) Have at least one year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of parasitology;

(f)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(f)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(f)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of parasitology; or

(f)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(f)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of parasitology; or

(f)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and

(f)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of parasitology.

(g) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of virology, the individual functioning as the technical supervisor must--

(g)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(g)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(g)(1)(ii)

See §493.1449(b)(2) Guidelines.

(g)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(g)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of virology; or

(g)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(g)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(g)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of virology; or
(g)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and
(g)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of virology; or
(g)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and
(g)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing within the specialty of microbiology with a minimum of 6 months experience in high complexity testing within the subspecialty of virology.

(h) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the specialty of diagnostic immunology, the individual functioning as the technical supervisor must--

(h)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

Interpretative Guidelines §493.1449(h)(1)(i)

See §493.1449(b)(2) Guidelines.

(h)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

(h)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(h)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing for the specialty of diagnostic immunology; or

(h)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(h)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(h)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of diagnostic immunology; or

(h)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(h)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing for the specialty of diagnostic immunology; or

(h)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and

(h)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing for the specialty of diagnostic immunology.

(i) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the specialty of chemistry, the individual functioning as the technical supervisor must--

- (i)(1)(i) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and**
- (i)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or**

Interpretative Guidelines §493.1449 (i)(1)(ii)

See § 493.1449(b)(2) Guidelines.

- (i)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and**
- (i)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing for the specialty of chemistry; or**
- (i)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and**

Interpretative Guidelines §493.1449(i)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

- (i)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of chemistry; or**
- (i)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and**
- (i)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing for the specialty of chemistry; or**
- (i)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and**
- (i)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing for the specialty of chemistry.**
- (j) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the specialty of hematology, the individual functioning as the technical supervisor must--**
 - (j)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and**
 - (j)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or**

Interpretative Guidelines §493.1449 (j)(1)(ii)

See §493.1449(b)(2) Guidelines.

- (j)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and**
- (j)(2)(ii) Have at least one year of laboratory training or experience, or both, in high complexity testing for the specialty of hematology (for example, physicians certified either in hematology or hematology and medical oncology by the American Board of Internal Medicine); or**
- (j)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and**

Interpretative Guidelines §493.1449(j)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

- (j)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of hematology; or**
- (j)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and**
- (j)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing for the specialty of hematology; or**
- (j)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and**
- (j)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing for the specialty of hematology.**
- (k)(1) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of cytology, the individual functioning as the technical supervisor must--**
 - (k)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and**
 - (k)(1)(ii) Meet one of the following requirements--**
 - (k)(1)(ii)(A) Be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or**
 - (k)(1)(ii)(B) Be certified by the American Society of Cytology to practice cytopathology or possess qualifications that are equivalent to those required for such certification;**

Interpretative Guidelines §493.1449(k)(1)(ii)(A) or (B)
See §493.1449(b)(2) Guidelines.

- (k)(2) An individual qualified under Sec. 493.1449(b) or paragraph (k)(1) of this section may delegate some of the cytology technical supervisor responsibilities to an individual who is in the final year of full-time training leading to certification specified in paragraphs (b) or (k)(1)(ii)(A) of this section provided the technical supervisor qualified under Sec. 493.1449(b) or paragraph (k)(1) of this section remains ultimately responsible for ensuring that all of the responsibilities of the cytology technical supervisor are met.**
- (l) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of histopathology, the individual functioning as the technical supervisor must--**
 - (l)(1) Meet one of the following requirements:**
 - (l)(i)(A) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and**
 - (l)(1)(B) Be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification;**

Interpretative Guidelines §493.1449(l)(1)(i)(B)
See §493.1449(b)(2) Guidelines.

An individual who has successfully completed a training program in neuromuscular pathology approved by HHS may examine and provide reports for neuromuscular pathology. As of 7/03, HHS has approved The American Academy of Neurology Committee for Neuromuscular Pathology Training Program.

- (l)(1)(B)(ii) An individual qualified under §493.1449(b) or paragraph (l)(1) of this section may delegate to an individual who is a resident in a training program leading to certification specified in paragraph (b) or (l)(1)(i)(B) of this section, the responsibility for examination and interpretation of histopathology specimens.**
- (l)(2) For tests in dermatopathology, meet one of the following requirements:**
 - (l)(2)(i)(A) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located and--**

(l)(2)(i)(B) Meet one of the following requirements:

(l)(2)(i)(B)(1) Be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

(l)(2)(i)(B)(2) Be certified in dermatopathology by the American Board of Dermatology and the American Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

(l)(2)(i)(B)(3) Be certified in dermatology by the American Board of Dermatology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(l)(2)(i)(B)(1),(2), or (3).

See §493.1449(b)(2) Guidelines.

(l)(2)(ii) An individual qualified under §493.1449(b) or paragraph (l)(2)(i) of this section may delegate to an individual who is a resident in a training program leading to certification specified in paragraphs (b) or (l)(2)(i)(B) of this section, the responsibility for examination and interpretation of dermatopathology specimens.

(l)(3) For tests in ophthalmic pathology, meet one of the following requirements:

(l)(3)(i)(A) Be a doctor of medicine or doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located and--

(l)(3)(i)(B) Must meet one of the following requirements:

(l)(3)(i)(B)(1) Be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

(l)(3)(i)(B)(2) Be certified by the American Board of Ophthalmology or possess qualifications that are equivalent to those required for such certification and have successfully completed at least 1 year of formal post-residency fellowship training in ophthalmic pathology; or

Interpretative Guidelines §493.1449(l)(3)(i)(B)(1) or (2).

See §493.1449(b)(2) Guidelines.

(l)(3)(i)(B)(2)(ii) An individual qualified under §493.1449(b) or paragraph (1)(3)(i) of this section may delegate to an individual who is a resident in a training program leading to certification specified in paragraphs (b) or (1)(3)(i)(B) of this section, the responsibility for examination and interpretation of ophthalmic specimens; or

(m) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the subspecialty of oral pathology, the individual functioning as the technical supervisor must meet one of the following requirements:

(m)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located and--

(m)(1)(ii) Be certified in anatomic pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

(m)(2) Be certified in oral pathology by the American Board of Oral Pathology or possess qualifications for such certification; or

(m)(3) An individual qualified under §493.1449(b) or paragraph (m) (1) or (2) of this section may delegate to an individual who is a resident in a training program leading to certification specified in paragraphs (b) or (m) (1) or (2) of this section, the responsibility for examination and interpretation of oral pathology specimens.

(n) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the specialty of radioassay, the individual functioning as the technical supervisor must--

(n)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(n)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(n)(1)(ii)

See §493.1449(b)(2) Guidelines.

(n)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(n)(2)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing for the specialty of radiobioassay; or

(n)(3)(i) Have an earned doctoral degree in a chemical, physical, biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(n)(3)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(n)(3)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing within the specialty of radiobioassay; or

(n)(4)(i) Have earned a master's degree in a chemical, physical, biological or clinical laboratory science or medical technology from an accredited institution; and

(n)(4)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing for the specialty of radiobioassay; or

(n)(5)(i) Have earned a bachelor's degree in a chemical, physical or biological science or medical technology from an accredited institution; and

(n)(5)(ii) Have at least 4 years of laboratory training or experience, or both, in high complexity testing for the specialty of radiobioassay.

(o) If the laboratory performs tests in the specialty of histocompatibility, the individual functioning as the technical supervisor must either--

(o)(1)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(o)(1)(ii) Have training or experience that meets one of the following requirements:

(o)(1)(ii)(A) Have 4 years of laboratory training or experience, or both, within the specialty of histocompatibility; or

(o)(1)(ii)(B)(1) Have 2 years of laboratory training or experience, or both, in the specialty of general immunology; and

(o)(2) Have 2 years of laboratory training or experience, or both, in the specialty of histocompatibility; or

(o)(2)(i) Have an earned doctoral degree in a biological or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(o)(2)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(o)(2)(ii) Have training or experience that meets one of the following requirements:

(o)(2)(ii)(A) Have 4 years of laboratory training or experience, or both, within the specialty of histocompatibility; or

(o)(2)(ii)(B)(1) Have 2 years of laboratory training or experience, or both, in the specialty of general immunology; and

(o)(2)(ii)(B)(2) Have 2 years of laboratory training or experience, or both, in the specialty of histocompatibility.

(p) If the laboratory performs tests in the specialty of clinical cytogenetics, the individual functioning as the technical supervisor must--

(p)(1)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(p)(1)(ii) Have 4 years of training or experience, or both, in genetics, 2 of which have been in clinical cytogenetics; or

(p)(2)(i) Hold an earned doctoral degree in a biological science, including biochemistry, or clinical laboratory science from an accredited institution; and

Interpretative Guidelines §493.1449(p)(2)(i)

See §493.2 for the definition of and guidance for accredited institutions.

(p)(2)(ii) Have 4 years of training or experience, or both, in genetics, 2 of which have been in clinical cytogenetics.

(q) If the requirements of paragraph (b) of this section are not met and the laboratory performs tests in the specialty of immunohematology, the individual functioning as the technical supervisor must--

(q)(1)(i) Be a doctor of medicine or a doctor of osteopathy licensed to practice medicine or osteopathy in the State in which the laboratory is located; and

(q)(1)(ii) Be certified in clinical pathology by the American Board of Pathology or the American Osteopathic Board of Pathology or possess qualifications that are equivalent to those required for such certification; or

Interpretative Guidelines §493.1449(q)(1)(ii)

See §493.1449(b)(2) Guidelines.

(q)(2)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located; and

(q)(2)(ii) Have at least one year of laboratory training or experience, or both, in high complexity testing for the specialty of immunohematology.

Note: The technical supervisor requirements for "laboratory training or experience, or both" in each specialty or subspecialty may be acquired concurrently in more than one of the specialties or subspecialties of service. For example, an individual, who has a doctoral degree in chemistry and additionally has documentation of 1 year of laboratory experience working concurrently in high complexity testing in the specialties of microbiology and chemistry and 6 months of that work experience included high complexity testing in bacteriology, mycology, and mycobacteriology, would qualify as the technical supervisor for the specialty of chemistry and the subspecialties of bacteriology, mycology, and mycobacteriology.

D6112

§493.1451 Standard: Technical supervisor responsibilities.

The technical supervisor is responsible for the technical and scientific oversight of the laboratory. The technical supervisor is not required to be on site at all times testing is performed; however, he or she must be available to the laboratory on an as needed basis to provide supervision as specified in (a) of this section.

Interpretative Guidelines §493.1451

In a specialty in which neither the director nor the general supervisor can qualify to provide technical supervision, the laboratory may engage the services of a qualified person either on a part-time or full-time basis for this service. The technical supervisor is not required to be on the premises full-time or at all times tests are being performed in

his/her specialty(ies). However, the technical supervisor must be available to provide consultation and is required to spend an amount of time in the laboratory sufficient to supervise the technical performance of the staff in his/her specialty(ies). There should be documentation, such as a log book or notes from training which indicate the technical supervisor performs his/her assigned duties. The technical supervisor is responsible for evaluating the capabilities of the testing personnel and the general supervisor's testing performance.

D6113

§493.1451 Standard: Technical supervisor responsibilities.

(a) The technical supervisor must be accessible to the laboratory to provide on-site, telephone, or electronic consultation; and

D6114

§493.1451 Standard: Technical supervisor responsibilities.

(b) The technical supervisor is responsible for--

(b)(1) Selection of the test methodology that is appropriate for the clinical use of the test results;

D6115

§493.1451 Standard: Technical supervisor responsibilities.

(b)(2) Verification of the test procedures performed and establishment of the laboratory's test performance characteristics, including the precision and accuracy of each test and test system;

D6116

§493.1451 Standard: Technical supervisor responsibilities.

(b)(3) Enrollment and participation in an HHS approved proficiency testing program commensurate with the services offered;

D6117

§493.1451 Standard: Technical supervisor responsibilities.

(b)(4) Establishing a quality control program appropriate for the testing performed and establishing the parameters for acceptable levels of analytic performance and ensuring that these levels are maintained throughout the entire testing process from the initial receipt of the specimen, through sample analysis and reporting of test results;

D6118

§493.1451 Standard: Technical supervisor responsibilities.

(b)(5) Resolving technical problems and ensuring that remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications;

D6119

§493.1451 Standard: Technical supervisor responsibilities.

(b)(6) Ensuring that patient test results are not reported until all corrective actions have been taken and the test system is functioning properly;

D6120

§493.1451 Standard: Technical supervisor responsibilities.

(b)(7) Identifying training needs and assuring that each individual performing tests receives regular in-service training and education appropriate for the type and complexity of the laboratory services performed;

Interpretative Guidelines §493.1451(b)(7)

In some instances, in-service training may be specifically related to an instrument or test, or may be very general in nature. The laboratory may establish its own format, content, and schedule or provide training on an as-needed basis. This is acceptable provided the laboratory does not have deficiencies related to test performance.

(b)(8) Evaluating the competency of all testing personnel and assuring that the staff maintain their competency to perform test procedures and report test results promptly, accurately and proficiently.

Probes §493.1451(b)(8)

What mechanism is used to ensure that testing personnel are following the laboratory's policies and procedures? When approved by the director, these policies and procedures may include manufacturer's instructions.

D6121

§493.1451 Standard: Technical supervisor responsibilities.

The procedures for evaluation of the competency of the staff must include, but are not limited to--

(b)(8)(i) Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing and testing;

D6122

§493.1451 Standard: Technical supervisor responsibilities.

(b)(8)(ii) Monitoring the recording and reporting of test results;

D6123

§493.1451 Standard: Technical supervisor responsibilities.

(b)(8)(iii) Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records;

D6124

§493.1451 Standard: Technical supervisor responsibilities.

(b)(8)(iv) Direct observation of performance of instrument maintenance and function checks;

D6125

§493.1451 Standard: Technical supervisor responsibilities.

(b)(8)(v) Assessment of test performance through testing previously analyzed specimens, internal blind testing samples or external proficiency testing samples; and

D6126

§493.1451 Standard: Technical supervisor responsibilities.

(b)(8)(vi) Assessment of problem solving skills; and

D6127

§493.1451 Standard: Technical supervisor responsibilities.

(b)(9) Evaluating and documenting the performance of individuals responsible for high complexity testing at least semiannually during the first year the individual tests patient specimens.

D6128

§493.1451 Standard: Technical supervisor responsibilities.

Thereafter, evaluations must be performed at least annually

D6129

§493.1451 Standard: Technical supervisor responsibilities.

unless test methodology or instrumentation changes, in which case, prior to reporting patient test results, the individual's performance must be reevaluated to include the use of the new test methodology or instrumentation.

(c) In cytology, the technical supervisor or the individual qualified under §493.1449(k)(2)--
(c)(1) May perform the duties of the cytology general supervisor and the cytotechnologist, as specified in §§493.1471 and 493.1485, respectively;

D6130

§493.1451 Standard: Technical supervisor responsibilities.

- (c)(2) Must establish the workload limit for each individual examining slides;
(c)(3) Must reassess the workload limit for each individual examining slides at least every 6 months and adjust as necessary;
-

D6131

§493.1451 Standard: Technical supervisor responsibilities.

- (c)(4) Must perform the functions specified in §493.1274(d) and (e);
-

D6132

§493.1451 Standard: Technical supervisor responsibilities.

- (c)(5) Must ensure that each individual examining gynecologic preparations participates in an HHS approved cytology proficiency testing program, as specified in §493.945 and achieves a passing score, as specified in §493.855; and
-

D6133

§493.1451 Standard: Technical supervisor responsibilities.

- (c)(6) If responsible for screening cytology slide preparations, must document the number of cytology slides screened in 24 hours and the number of hours devoted during each 24-hour period to screening cytology slides.
-

D6134

§493.1453 Condition: Laboratories performing high complexity testing; clinical consultant.

The laboratory must have a clinical consultant who meets the requirements of §493.1455 of this subpart and provides clinical consultation in accordance with §493.1457 of this subpart.

Interpretative Guidelines §493.1453

The Condition of clinical consultant is not met when the clinical consultant:

- *Position is not filled;*
 - *Is not qualified; or*
 - *Does not fulfill the clinical consultant responsibilities.*
-

D6135

§493.1455 Standard; Clinical consultant qualifications.

The clinical consultant must be qualified to consult with and render opinions to the laboratory's clients concerning the diagnosis, treatment and management of patient care. The clinical consultant must--

- (a) Be qualified as a laboratory director under §493.1443(b)(1), (2), or (3)(i) or, for the subspecialty of oral pathology, §493.1443(b)(6); or

(b) Be a doctor of medicine, doctor of osteopathy, doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located.

D6136

§493.1457 Standard; Clinical consultant responsibilities.

The clinical consultant provides consultation regarding the appropriateness of the testing ordered and interpretation of test results.

D6137

§493.1457 Standard; Clinical consultant responsibilities.

The clinical consultant must--

(a) Be available to provide consultation to the laboratory's clients;

D6138

§493.1457 Standard; Clinical consultant responsibilities.

(b) Be available to assist the laboratory's clients in ensuring that appropriate tests are ordered to meet the clinical expectations;

D6139

§493.1457 Standard; Clinical consultant responsibilities.

(c) Ensure that reports of test results include pertinent information required for specific patient interpretation; and

D6140

§493.1457 Standard; Clinical consultant responsibilities.

(d) Ensure that consultation is available and communicated to the laboratory's clients on matters related to the quality of the test results reported and their interpretation concerning specific patient conditions.

D6141

§493.1459 Condition: Laboratories performing high complexity testing; general supervisor.

The laboratory must have one or more general supervisors who are qualified under §493.1461 of this subpart to provide general supervision in accordance with §493.1463 of this subpart.

Interpretative Guidelines §493.1459

The Condition of general supervisor is not met when the general supervisor:

- *Position is not filled;*
- *Is not qualified; or*

- Does not fulfill the general supervisor responsibilities.

D6142

§493.1461 Standard; General supervisor qualifications.

The laboratory must have one or more general supervisors who, under the direction of the laboratory director and supervision of the technical supervisor, provides day-to-day supervision of testing personnel and reporting of test results. In the absence of the director and technical supervisor, the general supervisor must be responsible for the proper performance of all laboratory procedures and reporting of test results.

Interpretive Guidelines §493.1461

The type of experience required under this regulation is clinical in nature. This means examination and test performance on human specimens for purposes of obtaining information for the diagnosis, treatment, and monitoring of patients, or for providing information to others who will do the diagnosing and treating of the patient's condition.

Teaching experience directly related to a medical technology program, clinical laboratory sciences program, or a clinical laboratory section of a residency program is considered acceptable experience. Research experience is also acceptable experience if it is obtained while performing tests on human specimens. A year of laboratory training and experience is equivalent to 2080 hours and could extend over more than one 12 calendar-month period.

If all testing personnel have associate degrees, but none meet the training or experience requirement for general supervisor, the duties of the general supervisor must be fulfilled by an appropriately qualified individual. This individual need not be on-site at all times.

D6143

§493.1461 Standard: General supervisor qualifications.

- (a) The general supervisor must possess a current license issued by the State in which the laboratory is located, if such licensing is required; and
- (b) The general supervisor must be qualified as a--
 - (b)(1) Laboratory director under §493.1443; or
 - (b)(2) Technical supervisor under §493.1449.
- (c) If the requirements of paragraph (b)(1) or paragraph (b)(2) of this section are not met, the individual functioning as the general supervisor must--
 - (c)(1)(i) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located or have earned a doctoral, master's, or bachelor's degree in a chemical, physical, biological or clinical laboratory science, or medical technology from an accredited institution; and

Interpretative Guidelines §493.1461(c)(1)(i)

See §493.2 for the definition of and guidance for accredited institutions.

- (c)(1)(ii) Have at least 1 year of laboratory training or experience, or both, in high complexity testing; or
- (c)(2)(i) Qualify as testing personnel under §493.1489(b)(2); and
- (c)(2)(ii) Have at least 2 years of laboratory training or experience, or both, in high complexity testing; or

(c)(3)(i) Except as specified in paragraph (3)(ii) of this section, have previously qualified as a general supervisor under §493.1462 on or before February 28, 1992.

(c)(3)(ii) Exception. An individual who achieved a satisfactory grade in a proficiency examination for technologist given by HHS between March 1, 1986 and December 31, 1987, qualifies as a general supervisor if he or she meets the requirements of §493.1462 on or before January 1, 1994."

(c)(4) On or before September 1, 1992, have served as a general supervisor of high complexity testing and as of April 24, 1995--

(c)(4)(i) Meet one of the following requirements:

(c)(4)(i)(A) Have graduated from a medical laboratory or clinical laboratory training program approved or accredited by the Accrediting Bureau of Health Education Schools (ABHES), the Commission on Allied Health Education Accreditation (CAHEA), or other organization approved by HHS.

(c)(4)(i)(B) Be a high school graduate or equivalent and have successfully completed an official U.S. military medical laboratory procedures course of at least 50 weeks duration and have held the military enlisted occupational specialty of Medical Laboratory Specialist (Laboratory Technician).

(c)(4)(ii) Have at least 2 years of clinical laboratory training, or experience, or both, in high complexity testing; or

(c)(5) On or before September 1, 1992, have served as a general supervisor of high complexity testing and--

(c)(5)(i) Be a high school graduate or equivalent; and

(c)(5)(ii) Have had at least 10 years of laboratory training or experience, or both, in high complexity testing, including at least 6 years of supervisory experience between September 1, 1982 and September 1, 1992.

(d) For blood gas analysis, the individual providing general supervision must--

(d)(1) Be qualified under §§493.1461(b)(1) or (2), or 493.1461(c); or

(d)(2)(i) Have earned a bachelor's degree in respiratory therapy or cardiovascular technology from an accredited institution; and

(d)(2)(ii) Have at least one year of laboratory training or experience, or both, in blood gas analysis; or

(d)(3)(i) Have earned an associate degree related to pulmonary function from an accredited institution; and

Interpretative Guidelines §493.1461(d)(3)(i)

NOTE: Many blood gas systems are categorized as moderate complexity tests; therefore, only moderate complexity personnel requirements are applicable. To determine which tests are categorized as waived or nonwaived (i.e., moderate or high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/clia/index.html]. Test systems, assays, and examinations not yet classified are considered high complexity.

(d)(3)(ii) Have at least two years of training or experience, or both in blood gas analysis.

(e) The general supervisor requirement is met in histopathology, oral pathology, dermatopathology, and ophthalmic pathology because all tests and examinations, must be performed:

(e)(1) In histopathology, by an individual who is qualified as a technical supervisor under §§493.1449(b) or 493.1449(l)(1);

(e)(2) In dermatopathology, by an individual who is qualified as a technical supervisor under §§493.1449(b) or 493.1449(l) or (2);

(e)(3) In ophthalmic pathology, by an individual who is qualified as a technical supervisor under §§493.1449(b) or 493.1449(1)(3); and

(e)(4) In oral pathology, by an individual who is qualified as a technical supervisor under §§493.1449(b) or 493.1449(m).

Interpretative Guidelines §493.1461(e)

In the case of gross examinations, the technical supervisor may delegate to individuals qualified under §493.1489 the responsibility for the physical examination/description, including color, weight, measurement and other characteristics of the tissue; or other mechanical procedures for which a specific written protocol has been developed.

The technical supervisor is ultimately responsible for the diagnosis related to the gross examination and must sign the examination report. The technical supervisor is not required to provide direct onsite supervision but is responsible for the accuracy of all test results reported. All physical examinations/descriptions of tissue including color, weight, measurement and other characteristics of the tissue; or other mechanical procedures performed in the absence of the technical supervisor by individuals qualified under §493.1489 should be reviewed within 24 hours by the technical supervisor. All microscopic tissue examinations must be performed by individuals qualified under §493.1449(b), (l) or (m), as appropriate.

§493.1462 General supervisor qualifications on or before February 28, 1992.

To qualify as a general supervisor under §493.1461(c)(3), an individual must have met or could have met the following qualifications as they were in effect on or before February 28, 1992.

(a) Each supervisor possesses a current license as a laboratory supervisor issued by the State, if such licensing exists; and

(b) The laboratory supervisor--

(b)(1) Who qualifies as a laboratory director under §493.1406(b)(1), (2), (4), or (5) is also qualified as a general supervisor; therefore, depending upon the size and functions of the laboratory, the laboratory director may also serve as the laboratory supervisor; or

(b)(2)(i) Is a physician or has earned a doctoral degree from an accredited institution with a major in one of the chemical, physical, or biological sciences; and

(b)(2)(ii) Subsequent to graduation, has had at least 2 years of experience in one of the laboratory specialties in a laboratory; or

(b)(3)(i) Holds a master's degree from an accredited institution with a major in one of the chemical, physical, or biological sciences; and

(b)(3)(ii) Subsequent to graduation has had at least 4 years of pertinent full-time laboratory experience of which not less than 2 years have been spent working in the designated specialty in a laboratory; or

(b)(4)(i) Is qualified as a laboratory technologist under §493.1491; and

(b)(4)(ii) After qualifying as a laboratory technologist, has had at least 6 years of pertinent full-time laboratory experience of which not less than 2 years have been spent working in the designated laboratory specialty in a laboratory; or

(b)(5) With respect to individuals first qualifying before July 1, 1971, has had at least 15 years of pertinent full-time laboratory experience before January 1, 1968; this required experience may be met by the substitution of education for experience.

D6144

§493.1463 Standard; General supervisor responsibilities.

The general supervisor is responsible for day-to-day supervision or oversight of the laboratory operation and personnel performing testing and reporting test results.

Interpretative Guidelines §493.1463

Interview several testing personnel to elicit information about the duties they perform and the degree of supervision they receive.

D6145

§493.1463 Standard; General supervisor responsibilities.

(a) The general supervisor--(a)(1) Must be accessible to testing personnel at all times testing is performed to provide on-site, telephone or electronic consultation to resolve technical problems in accordance with policies and procedures established either by the laboratory director or technical supervisor;

D6146

§493.1463 Standard; General supervisor responsibilities.

(a)(2) Is responsible for providing day-to-day supervision of high complexity test performance by a testing personnel qualified under §493.1489;

D6147

§493.1463 Standard; General supervisor responsibilities.

(a)(3) Except as specified in paragraph (c) of this section, must be onsite to provide direct supervision when high complexity testing is performed by any individuals qualified under §493.1489(b)(5); and

D6148

§493.1463 Standard; General supervisor responsibilities.

(a)(4) Is responsible for monitoring test analyses and specimen examinations to ensure that acceptable levels of analytic performance are maintained.

D6149

§493.1463 Standard; General supervisor responsibilities.

(b) The director or technical supervisor may delegate to the general supervisor the responsibility for--

(b)(1) Assuring that all remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications;

D6150

§493.1463 Standard; General supervisor responsibilities.

(b)(2) Ensuring that patient test results are not reported until all corrective actions have been taken and the test system is properly functioning;

D6151

§493.1463 Standard; General supervisor responsibilities.

- (b)(3) Providing orientation to all testing personnel; and
(b)(4) Annually evaluating and documenting the performance of all testing personnel.
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D6152

§493.1463 Standard; General supervisor responsibilities.

(c) Exception. For individuals qualified under §493.1489(b)(5), who were performing high complexity testing on or before January 19, 1993, the requirements of paragraph (a)(3) of this section are not effective, provided that all high complexity testing performed by the individual in the absence of a general supervisor is reviewed within 24 hours by a general supervisor qualified under §493.1461.

D6153

§493.1467 Condition: Laboratories performing high complexity testing; cytology general supervisor.

For the subspecialty of cytology, the laboratory must have a general supervisor who meets the qualification requirements of §493.1469 of this subpart, and provides supervision in accordance with §493.1471 of this subpart.

Interpretative Guideline §493.1467

The Condition of cytology general supervisor is not met when the cytology general supervisor:

- *Position is not filled;*
 - *Is not qualified; or*
 - *Does not fulfill the cytology general supervisor responsibilities.*
-

D6155

§493.1469 Standard; Cytology general supervisor qualifications.

The cytology general supervisor must be qualified to supervise cytology services. The general supervisor in cytology must possess a current license issued by the State in which the laboratory is located, if such licensing is required, and must--

- (a) Be qualified as a technical supervisor under §493.1449 (b) or (k); or
(b)(1) Be qualified as a cytotechnologist under §493.1483; and
(b)(2) Have at least 3 years of full-time (2,080 hours per year) experience as a cytotechnologist within the preceding 10 years.

Interpretative Guidelines §493.1469(b)(2)

In addition to screening slides in a laboratory, the 3 years of full-time experience as a cytotechnologist can be fulfilled if the individual has been:

- *Teaching in schools of cytotechnology;*
 - *Teaching cytotechnology for residency programs in academic institutions; or*
 - *Participating in research directly related to cytotechnology, which includes screening slides, library research, and documentation.*
-

D6156

§493.1471 Standard; Cytology general supervisor responsibilities.

The technical supervisor of cytology may perform the duties of the cytology general supervisor or delegate the responsibilities to an individual qualified under §493.1469.

D6157

§493.1471 Standard; Cytology general supervisor responsibilities.

(a) The cytology general supervisor is responsible for the day-to-day supervision or oversight of the laboratory operation and personnel performing testing and reporting test results.

D6158

§493.1471 Standard; Cytology general supervisor responsibilities.

(b) The cytology general supervisor must--

(b)(1) Be accessible to provide on-site, telephone, or electronic consultation to resolve technical problems in accordance with policies and procedures established by the technical supervisor of cytology;

D6159

§493.1471 Standard; Cytology general supervisor responsibilities.

(b)(2) Document the slide interpretation results of each gynecologic and nongynecologic cytology case he or she examined or reviewed (as specified under §493.1274(c));

D6160

§493.1471 Standard; Cytology general supervisor responsibilities.

(b)(3) For each 24-hour period, document the total number of slides he or she examined or reviewed in the laboratory as well as the total number of slides examined or reviewed in any other laboratory or for any other employer; and

D6161

§493.1471 Standard; Cytology general supervisor responsibilities.

(b)(4) Document the number of hours spent examining slides in each 24-hour period.

D6162

§493.1481 Condition: Laboratories performing high complexity testing; cytotechnologist.

For the subspecialty of cytology, the laboratory must have a sufficient number of cytotechnologists who meet the qualifications specified in §493.1483 to perform the functions specified in §493.1485.

D6163

§493.1483 Standard; Cytotechnologist qualifications.

Each person examining cytology slide preparations must meet the qualifications of §493.1449 (b) or (k), or--

D6164

§493.1483 Standard; Cytotechnologist qualifications.

- (a) Possess a current license as a cytotechnologist issued by the State in which the laboratory is located, if such licensing is required; and
- (b) Meet one of the following requirements:
 - (b)(1) Have graduated from a school of cytotechnology accredited by the Committee on Allied Health Education and Accreditation or other organization approved by HHS; or
 - (b)(2) Be certified in cytotechnology by a certifying agency approved by HHS; or
 - (b)(3) Before September 1, 1992--
 - (b)(3)(i) Have successfully completed 2 years in an accredited institution with at least 12 semester hours in science, 8 hours of which are in biology; and
 - (b)(3)(i)(A) Have had 12 months of training in a school of cytotechnology accredited by an accrediting agency approved by HHS; or

Interpretative Guideline §493.1483(b)(3)(i)(A)

"A school of cytotechnology accredited by an accrediting agency approved by HHS" means a school or program approved by one of the accrediting agencies described in Subpart A of the Guidelines. (See §493.2)

- (b)(3)(i)(B) Have received 6 months of formal training in a school of cytotechnology accredited by an accrediting agency approved by HHS and 6 months of full-time experience in cytotechnology in a laboratory acceptable to the pathologist who directed the formal 6 months of training; or
 - (b)(3)(ii) Have achieved a satisfactory grade to qualify as a cytotechnologist in a proficiency examination approved by HHS and designed to qualify persons as cytotechnologists; or
 - (b)(4) Before September 1, 1994, have full-time experience of at least 2 years or equivalent within the preceding 5 years examining slide preparations under the supervision of a physician qualified under §493.1449(b) or (k)(1), and before January 1, 1969, must have--
 - (b)(4)(i) Graduated from high school;
 - (b)(4)(ii) Completed 6 months of training in cytotechnology in a laboratory directed by a pathologist or other physician providing cytology services; and
 - (b)(4)(iii) Completed 2 years of full-time supervised experience in cytotechnology; or
 - (b)(5)(i) On or before September 1, 1994, have full-time experience of at least 2 years or equivalent examining cytology slide preparations within the preceding 5 years in the United States under the supervision of a physician qualified under §493.1449(b) or (k)(1); and
 - (b)(5)(ii) On or before September 1, 1995, have met the requirements in either paragraph (b)(1) or (2) of this section.
-

D6165

§493.1485 Standard; Cytotechnologist responsibilities.

The cytotechnologist is responsible for documenting--

(a) The slide interpretation results of each gynecologic and nongynecologic cytology case he or she examined or reviewed (as specified in §493.1274(c));

D6166

§493.1485 Standard; Cytotechnologist responsibilities.

(b) For each 24-hour period, the total number of slides examined or reviewed in the laboratory as well as the total number of slides examined or reviewed in any other laboratory or for any other employer; and

D6167

§493.1485 Standard; Cytotechnologist responsibilities.

(c) The number of hours spent examining slides in each 24-hour period.

D6168

§493.1487 Condition: Laboratories performing high complexity testing; testing personnel.

The laboratory has a sufficient number of individuals who meet the qualification requirements of §493.1489 of this subpart to perform the functions specified in §493.1495 of this subpart for the volume and complexity of testing performed.

Interpretative Guidelines §493.1487

The criteria used to determine the adequacy of the testing personnel involves evaluating testing personnel responsibilities, ensuring that these responsibilities are specified by the director in writing and are appropriate to ensure compliance with the reporting and recordkeeping requirements, quality control monitoring, quality assessment activities, and proficiency testing participation. Cite this deficiency only when problems are found in areas that can be directly related to insufficient numbers of testing personnel. (Use D6101 to relate the finding to insufficient personnel to director responsibilities.)

D6170

§493.1489 Standard; Testing personnel qualifications.

Each individual performing high complexity testing must--

(a) Possess a current license issued by the State in which the laboratory is located, if such licensing is required; and

D6171

§493.1489 Standard; Testing personnel qualifications.

(b) Meet one of the following requirements:

(b)(1) Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the State in which the laboratory is located or have earned a doctoral, master's or bachelor's degree in a chemical, physical, biological or clinical laboratory science, or medical technology from an accredited institution;

Interpretative Guidelines §493.1489(b)(1)

See §493.2 for the definition of and guidance for accredited institutions.

(b)(2)(i) Have earned an associate degree in a laboratory science, or medical laboratory technology from an accredited institution or--

Interpretative Guidelines §493.1489(b)(2)

"An associate degree in a laboratory science" is interpreted to mean an associate degree in a chemical or biological science.

(b)(2)(ii) Have education and training equivalent to that specified in paragraph (b)(2)(i) of this section that includes--

(b)(2)(ii)(A) At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, include either--

(b)(2)(ii)(A)(1) 24 semester hours of medical laboratory technology courses; or

(b)(2)(ii)(A)(2) 24 semester hours of science courses that include--

(b)(2)(ii)(A)(2)(i) Six semester hours of chemistry;

(b)(2)(ii)(A)(2)(ii) Six semester hours of biology; and

(b)(2)(ii)(A)(2)(iii) Twelve semester hours of chemistry, biology, or medical laboratory technology in any combination; and

(b)(2)(ii)(B) Have laboratory training that includes either of the following:

(b)(2)(ii)(B)(1) Completion of a clinical laboratory training program approved or accredited by the ABHES, the CAHEA, or other organization approved by HHS. (This training may be included in the 60 semester hours listed in paragraph (b)(2)(ii)(A) of this section.)

(b)(2)(ii)(B)(2) At least 3 months documented laboratory training in each specialty in which the individual performs high complexity testing.

(b)(3) Have previously qualified or could have qualified as a technologist under §493.1491 on or before February 28, 1992;

(b)(4) On or before April 24, 1995 be a high school graduate or equivalent and have either--

(b)(4)(i) Graduated from a medical laboratory or clinical laboratory training program approved or accredited by ABHES, CAHEA, or other organization approved by HHS; or

(b)(4)(ii) Successfully completed an official U.S. military medical laboratory procedures training course of at least 50 weeks duration and have held the military enlisted occupational specialty of Medical Laboratory Specialist (Laboratory Technician);

(b)(5)(i) Until September 1, 1997--

(b)(5)(i)(A) Have earned a high school diploma or equivalent; and

(b)(5)(i)(B) Have documentation of training appropriate for the testing performed before analyzing patient specimens. Such training must ensure that the individual has--

(b)(5)(i)(B)(1) The skills required for proper specimen collection, including patient preparation, if applicable, labeling, handling, preservation or fixation, processing or preparation, transportation and storage of specimens;

(b)(5)(i)(B)(2) The skills required for implementing all standard laboratory procedures;

(b)(5)(i)(B)(3) The skills required for performing each test method and for proper instrument use;

(b)(5)(i)(B)(4) The skills required for performing preventive maintenance, troubleshooting, and calibration procedures related to each test performed;

(b)(5)(i)(B)(5) A working knowledge of reagent stability and storage;

(b)(5)(i)(B)(6) The skills required to implement the quality control policies and procedures of the laboratory;

(b)(5)(i)(B)(7) An awareness of the factors that influence test results; and

(b)(5)(i)(B)(8) The skills required to assess and verify the validity of patient test results through the evaluation of quality control values before reporting patient test results; and

(b)(5)(ii) As of September 1, 1997, be qualified under §493.1489(b)(1), (b)(2), or (b)(4), except for those individuals qualified under paragraph (b)(5)(i) of this section who were performing high complexity testing on or before April 24, 1995;

Interpretative Guidelines §493.1489(b)(5)(ii)

The laboratory director is responsible for ensuring that testing personnel have the appropriate education and experience, and receive the appropriate training for the type and complexity of testing performed. The experience required is clinical in nature. This means examination of and test performance on human specimens for purposes of obtaining information for the diagnosis, treatment, and monitoring of patients, or for providing information to others who will do the diagnosing and treating of the patient's condition. (Use D6102.)

Each individual must have documentation of training applicable to the types and complexity of testing performed. This training should be such that the individual can demonstrate that he/she has the skills required for proper performance of preanalytic, analytic, and postanalytic phases of testing. For example, if the individual performs a manual differential, he/she should be able to demonstrate the skills for:

- Proper specimen handling prior to testing, e.g., assuring the specimen is properly drawn, if appropriate, properly labeled, the blood film is made within appropriate timeframes and is one-cell layer thick and without cell distortion;
- Proper test performance according to the laboratory's policies and manufacturer's instructions, e.g., using stains that are not outdated, that lack contamination and precipitation, following staining procedures, including staining order and timing and allowing slide to air dry, identification of cells and interpretation of smear to be consistent with blood count, diagnosis, treatment; and
- Proper reporting of patient test results in accordance with the laboratory's policies, e.g., notifying the person authorized to receive test results of a panic value, not reporting the test result if inconsistent with blood count and noting an explanation, such as "platelet clumping."

Training may include, but is not limited to, attendance at:

- Seminars given by experts in the field, e.g., a lecture about antibiotic resistance given by the infection control officer of a local hospital;
- On-site or off-site instrument trainings given by a manufacturer, e.g., a week-long training course given at the manufacturer's headquarters, or training by a manufacturer's technical representative on an instrument purchased by a laboratory;
- Technical training sessions, workshops, or conferences given by a professional laboratory organization, e.g., CAP, ASMT, AACC, and ASCT;
- Technical education classes or specialty courses that include hands-on test performance, e.g., parasitology, bacteriology, cytology, given by CDC, a State Health Department, or professional laboratory organizations;
- A formal laboratory training program; or
- In-services offered by a local hospital laboratory staff, pathologist, or medical technologist to a physician's office personnel.

Documentation may consist of, but is not limited to, letters from training programs or employers, attestation statements by the laboratory director, a log sheet initialed by the attendees indicating attendance at a training session/in-service, certificates from organizations providing the training session, workshop, conference, or specialty course.

(b)(6) For blood gas analysis--

Interpretative Guidelines §493.1489(b)(6)

This requirement applies only to performance of blood gas analysis procedures which are categorized as high complexity.

NOTE: Some blood gas systems are categorized as moderate complexity tests. Therefore, only moderate complexity personnel requirements are applicable to them. To determine which tests are categorized as waived or nonwaived (i.e., moderate or high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/clia/index.html]. Test systems, assays, and examinations not yet classified are considered high complexity.

- (b)(6)(i) Be qualified under §493.1489(b)(1), (b)(2), (b)(3), (b)(4), or (b)(5);**
- (b)(6)(ii) Have earned a bachelor's degree in respiratory therapy or cardiovascular technology from an accredited institution; or**
- (b)(6)(iii) Have earned an associate degree related to pulmonary function from an accredited institution; or**
- (b)(7) For histopathology, meet the qualifications of §493.1449 (b) or (l) to perform tissue examinations.**

Interpretative Guidelines §493.1489(b)(7)

In the case of gross examinations, the technical supervisor may delegate to individuals qualified under §493.1489 the responsibility for the physical examination/description, including color, weight, measurement and other characteristics of the tissue; or other mechanical procedures for which a specific written protocol has been developed. The technical supervisor is ultimately responsible for the diagnosis related to the gross examination and must sign the examination report. The technical supervisor is not required to provide direct onsite supervision but is responsible for the accuracy of all test results reported. All physical examinations/descriptions of tissue including color, weight, measurement and other characteristics of the tissue; or other mechanical procedures performed in the absence of the technical supervisor by individuals qualified under §493.1489 should be reviewed within 24 hours by the technical supervisor. All microscopic tissue examinations must be performed by individuals qualified under §493.1449(b), (l) or (m), as appropriate.

§493.1491 Technologist qualifications on or before February 28, 1992.

In order to qualify as high complexity testing personnel under §493.1489(b)(3), the individual must have met or could have met the following qualifications for technologist as they were in effect on or before February 28, 1992. Each technologist must--

- (a) Possess a current license as a laboratory technologist issued by the State, if such licensing exists; and**
- (b)(1) Have earned a bachelor's degree in medical technology from an accredited university; or**
- (b)(2) Have successfully completed 3 years of academic study (a minimum of 90 semester hours or equivalent) in an accredited college or university, which met the specific requirements for entrance into a school of medical technology accredited by an accrediting agency approved by the Secretary, and has successfully completed a course of training of at least 12 months in such a school; or**
- (b)(3) Have earned a bachelor's degree in one of the chemical, physical, or biological sciences and, in addition, has at least 1 year of pertinent full-time laboratory experience or training, or both, in the specialty or subspecialty in which the individual performs tests; or**
- (b)(4)(i) Have successfully completed 3 years (90 semester hours or equivalent) in an accredited college or university with the following distribution of courses--**
 - (b)(4)(i)(A) For those whose training was completed before September 15, 1963. At least 24 semester hours in chemistry and biology courses of which--**
 - (b)(4)(i)(A)(1) At least 6 semester hours were in inorganic chemistry and at least 3 semester hours were in other chemistry courses; and**

- (b)(4)(i)(A)(2) At least 12 semester hours in biology courses pertinent to the medical sciences; or
- (b)(4)(i)(B) For those whose training was completed after September 14, 1963.
- (b)(4)(i)(B)(1) 16 semester hours in chemistry courses that included at least 6 semester hours in inorganic chemistry and that are acceptable toward a major in chemistry;
- (b)(4)(i)(B)(2) 16 semester hours in biology courses that are pertinent to the medical sciences and are acceptable toward a major in the biological sciences; and
- (b)(4)(i)(B)(3) 3 semester hours of mathematics; and
- (b)(4)(ii) Has experience, training, or both, covering several fields of medical laboratory work of at least 1 year and of such quality as to provide him or her with education and training in medical technology equivalent to that described in paragraphs (b)(1) and (2) of this section; or
- (b)(5) With respect to individuals first qualifying before July 1, 1971, the technologist--
- (b)(5)(i) Was performing the duties of a laboratory technologist at any time between July 1, 1961, and January 1, 1968, and
- (b)(5)(ii) Has had at least 10 years of pertinent laboratory experience prior to January 1, 1968. (This required experience may be met by the substitution of education for experience); or
- (b)(6) Achieves a satisfactory grade in a proficiency examination approved by HHS.
-

D6173

§493.1495 Standard; Testing personnel responsibilities.

The testing personnel are responsible for specimen processing, test performance and for reporting test results.

D6174

§493.1495 Standard; Testing personnel responsibilities.

(a) Each individual performs only those high complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities.

D6175

§493.1495 Standard; Testing personnel responsibilities.

(b) Each individual performing high complexity testing must--

(b)(1) Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting and maintaining records of patient test results;

D6176

§493.1495 Standard; Testing personnel responsibilities.

(b)(2) Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens;

D6177

§493.1495 Standard; Testing personnel responsibilities.

(b)(3) Adhere to the laboratory's quality control policies, document all quality control activities, instrument and procedural calibrations and maintenance performed;

D6178

§493.1495 Standard; Testing personnel responsibilities.

(b)(4) Follow the laboratory's established policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance;

D6179

§493.1495 Standard; Testing personnel responsibilities.

(b)(5) Be capable of identifying problems that may adversely affect test performance or reporting of test results and either must correct the problems or immediately notify the general supervisor, technical supervisor, clinical consultant, or director;

Interpretative Guidelines §493.1495(b)(5) Guidelines:

If, during the survey, testing personnel demonstrate an inability to identify a problem that adversely affects a patient test result, cite 493.1445(e)(12) under the director responsibilities.

Some examples of problems that may adversely affect patient test results may include:

- *A pleural fluid that is mislabeled as a urine specimen and, therefore, is cultured as a urine culture;*
 - *Performing a potassium on a hemolyzed sample; or*
 - *Tests are incubated at 37°C when the manufacturer's instructions require 25°C incubation.*
-

D6181

§493.1495 Standard; Testing personnel responsibilities.

(b)(6) Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications; and

D6182

§493.1495 Standard; Testing personnel responsibilities.

(b)(7) Except as specified in paragraph (c) of this section, if qualified under §493.1489(b)(5), perform high complexity testing only under the onsite, direct supervision of a general supervisor qualified under §493.1461.

D6183

§493.1495 Standard; Testing personnel responsibilities.

(c) Exception. For individuals qualified under §493.1489(b)(5), who were performing high complexity testing on or before January 19, 1993, the requirements of paragraph (b)(7) of this section are not effective, provided that all high complexity testing performed by the

individual in the absence of a general supervisor is reviewed within 24 hours by a general supervisor qualified under §493.1461.

§493.1261 Standard: Bacteriology.
(Rev. 32, 02-13-2004)

(a) The laboratory must check the following for positive and negative reactivity using control organisms:

Interpretive Guidelines §493.1261(a)

When condition level deficiencies in Bacteriology are in any or all phases of testing, use D5002.

*For direct antigen systems, laboratories may use bacterial cell suspensions to meet the requirement for control organisms since the cell suspensions are subjected to both the extraction and reaction phases of the test. However, a matrix similar to patient specimens is preferred. For example, for direct antigen tests for group A streptococcal antigen, ready prepared, dried (solid-shafted) swabs, one containing group A streptococcus (*S. pyogenes*) as a positive control and another with non-group A streptococcus and/or *Staphylococcus aureus* as a negative control may be used. Use D5453 for deficiencies related to the extraction process.*

Additionally, if the manufacturer's instructions do not specify what the positive control contains, the laboratory should contact the manufacturer to ensure that the positive control contains a cell suspension of the organism. Otherwise, the laboratory must have an alternative mechanism for meeting this requirement (e.g., laboratory suspension stock ATCC organism, commercially prepared organism controls).

For microbial identification systems utilizing two or more substrates, the laboratory must check each media using control organisms to verify positive and negative reactivity of each substrate. Use D5471.

If a laboratory utilizes primary isolation media (e.g., MacConkey, CLED, EMB), for presumptive identification of organisms, then the media should meet the quality control requirements at D5471 and D5477.

For bacitracin, catalase, coagulase plasma, desoxycholate, oxidase, PYR disks, spot indole, staphylococcal latex reagents, streptococcal latex grouping reagents, and X and V factor strips and disks, use D5471.

For bacteriology, XV discs or strips need only be checked with an organism that produces a positive reaction. Use 5471.

For guidelines for molecular amplification testing, use D5455.

D5501

§493.1261 Standard: Bacteriology.

(a)(1) Each day of use for beta-lactamase methods other than Cefinase™.

Interpretive Guidelines §493.1261(a)(1)

Beta-lactamase testing performed by acidometric, iodometric or chromogenic methodologies other than Cefinase™ must have positive and negative reactivity checked each day of use.

For Cefinase™, use D5471.

D5503

§493.1261 Standard: Bacteriology.

(a)(2) Each week of use for Gram stains.

D5505

§493.1261 Standard: Bacteriology.

(a)(3) When each batch (prepared in-house), lot number (commercially prepared), and shipment of antisera is prepared or opened, and once every 6 months thereafter.

Interpretive Guidelines §493.1261(a)(3)

In addition to Salmonella and Shigella antisera, antisera used for serotyping of homologous isolates, (i.e., streptococcal serotyping systems) must be checked for positive and negative reactivity. Polyvalent antisera should be tested with at least one organism from each polyvalent group.

Requirements for antisera QC apply to testing that has a direct impact on patient care.

D5507

§493.1261 Standard: Bacteriology.

(b) For antimicrobial susceptibility tests, the laboratory must check each batch of media and each lot number and shipment of antimicrobial agent(s) before, or concurrent with, initial use, using approved control organisms.

(b)(1) Each day tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

(b)(2) The laboratory's zone sizes or minimum inhibitory concentration for control organisms must be within established limits before reporting patient results.

Interpretive Guidelines §493.1261(b)(1-2)

"Approved control organism(s)" means either an appropriate control strain or an equivalent strain as defined below.

The laboratory must ensure proper standardization of the inoculum (e.g., use a 0.5 McFarland standard or its optical equivalent, or follow manufacturer's instructions for a commercially available system). Use D5437.

ANTIMICROBIAL DISK DIFFUSION SUSCEPTIBILITY (BAUER, KIRBY, SHERRIS AND TURK METHOD)

Each new batch of medium and each new lot/shipment of antimicrobial disks must be checked as follows:

ANTIMICROBIAL DISK SUSCEPTIBILITY TEST

Appropriate Control Strain	Each New Batch of Media and Disks	Each Day If Isolates Are:
<u>S. aureus</u> ATCC 25923 or equivalent**	X	<u>Staphylococcus</u> spp.
<u>E. coli</u> ATCC 25922 or equivalent**	X	<u>Enterobacteriaceae</u>
<u>P. aeruginosa</u> ATCC 27853 and <u>E. coli</u> ATCC 25922 or equivalent**	X	<u>Pseudomonas aeruginosa</u> <u>Acintebacter</u> spp.

NOTE 1: Routine quality control testing of commercially prepared Mueller-Hinton agar for thymine and thymidine is not needed. However, if problems with quality control of sulfonamides and trimethoprim occur, the Mueller-Hinton agar should be checked with E. faecalis ATCC 29212 or alternatively, E. faecalis ATCC 33186 with trimethoprim-sulfamethoxazole disks. Satisfactory media will provide essentially clear distinct zones of inhibition 20 mm or greater in diameter. Unsatisfactory media will produce no zone of inhibition, growth within the zone, or a zone of less than 20 mm.

NOTE 2: If testing beta-lactam/beta-lactamase inhibitor antimicrobial agents (e.g., ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam, or ticarcillin-clavulanic acid), the laboratory should test E. coli ATCC 35218 (beta-lactamase producing strain).

NOTE 3: If performing extended spectrum beta-lactamase (ESBL) tests, the laboratory should test Klebsiella pneumoniae ATCC 700603 (ESBL-producing strain).

Zone sizes must be recorded for each antimicrobial control and limits must be established.

**An equivalent strain is one which demonstrates reactivity similar to an ATCC strain and for which limits have been established. Organisms which manufacturers recommend or require for use in their systems are acceptable strains of control organisms.

Refer to Table 3A*** of the NCCLS Standard, "Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard-Eighth Edition (M2-A8)" to determine the control strain to be used when performing antimicrobial disk susceptibility tests on isolates of Haemophilus spp., Neisseria gonorrhoeae, Streptococcus pneumoniae or other organisms as applicable.

When testing is performed daily, for each antimicrobial agent/organism combination, 1 out of every 20 consecutive results may be out of the acceptable range. Any more than 1 out-of-control result in 20 consecutive tests requires corrective action.

EXCEPTION: The laboratory may test each appropriate control strain a minimum of once each week, provided the following requirements are met:

The laboratory must document that appropriate control strains were tested for 20 or 30 consecutive test days. For each antimicrobial agent/organism combination, no more than one out of 20 or three out of the 30 zone diameters (i.e., zone diameters obtained from one antimicrobial agent-organism combination for 20 or 30 consecutive test days) may be

*outside established acceptable limits for quality control strains. These limits may be established by the laboratory, or the laboratory may use the acceptable ranges provided in Table 3*** and 3A*** of the NCCLS Standard, "Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard-Eighth Edition (M2-A8)."*

NOTE: This procedure is to be used for demonstrating satisfactory performance for conversion from daily to weekly quality control of the antimicrobial disk diffusion test.

After a laboratory has implemented weekly quality control testing of the disk diffusion test:

- *Quality control testing must be performed whenever any reagent component of the test is changed (e.g., a new lot of agar or a new lot of disks);*
- *Corrective action is required if any of the weekly quality control results are outside of the established acceptable range;*
- *If a new antimicrobial agent is added, it must be tested for 20 or 30 consecutive days and have satisfactory performance documented before it can be tested on a weekly schedule; and*
- *If there is a major change on the method of reading test results, such as conversion from manual zone measurements to an automated zone reader, 20 or 30 days of testing is required.*

If a zone diameter is observed outside the established acceptable limits for quality control strains during weekly quality control testing, the following corrective action(s) are necessary:

- *If there is an obvious reason for the out-of-control result (e.g., use of the wrong disk, use of the wrong control strain, obvious contamination of the strain, inadvertent use of the wrong incubation temperature or conditions), document the reason and retest the strain on the day the error is observed. If the repeat result is within range, no further corrective action is necessary.*
- *If there is not an obvious reason for the out-of-control result, test the implicated antimicrobial agent/organism combination on the day the error is observed and test for a total of 5 consecutive test days. If all 5 zone diameter measurements for the antimicrobial agent/organism combination are within the established acceptable ranges, no additional corrective action is necessary.*

For the last item mentioned above, if any of the 5 zone diameter measurements are outside the established acceptable range, additional corrective action is necessary. Daily control of tests must be continued until final resolution of the problem is achieved. Once the problem is corrected, in order to return to weekly quality control testing, documentation of satisfactory performance for another 20 or 30 consecutive days is required.

Direct susceptibility testing is a modification of the standardized disk diffusion susceptibility testing method. Therefore, the laboratory must establish the interpretive zone diameters for patient specimens, as well as establish the zone diameters for quality control organisms. Since direct susceptibility testing is not a recommended NCCLS method, the laboratory may not go to weekly quality control, but must perform quality control daily using appropriate control organisms.

MINIMUM INHIBITORY CONCENTRATION (MIC)

Each new batch of macrodilution tubes, microdilution trays, or agar dilution plates must be checked as follows:

MINIMUM INHIBITORY CONCENTRATION (MIC)

<i>Appropriate Control Strain</i>	<i>Each New Batch of Media</i>	<i>Each Day If Isolates are:</i>
<u><i>S. aureus</i></u> ATCC 29213 or equivalent**	X	<u><i>Staphylococcus</i></u> spp.
<u><i>E. coli</i></u> ATCC 25922 or equivalent**	X	<u>Enterobacteriaceae</u>
<u><i>P. aeruginosa</i></u> ATCC 27853 and <u><i>E. coli</i></u> ATCC 25922 or equivalent **	X	Non-Enterobacteriaceae to include <u><i>Acintebacter</i></u> spp., <u><i>Stenotrophomonas maltophilia</i></u> , <u><i>Pseudomonas</i></u> spp. and other nonfastidious, glucose nonfermenting, gram-negative bacilli
<u><i>E. faecalis</i></u> ATCC 29212 or equivalent**	X	<u>Enterococcus</u> spp.

NOTE 1: To determine the suitability of the Mueller-Hinton broth for sulfonamide and trimethoprim tests, MICs may be performed with *E. faecalis* ATCC 29212. Routine quality control testing of commercially manufactured panels for thymine and thymidine is not needed. However, should problems with QC of sulfonamides and trimethoprim occur, an MIC test should be performed with *E. faecalis* ATCC 29212 with trimethoprim-sulfamethoxazole. If the MIC for trimethoprim-sulfamethoxazole is < 0.5/9.5 ug/ml, the medium may be considered adequate.

NOTE 2: If testing beta-lactam/beta-lactamase inhibitor antimicrobial agents (e.g., ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam, or ticarcillin-clavulanic acid), the laboratory should test *E. coli* ATCC 35218.

NOTE 3: If performing extended spectrum beta-lactamase (ESBL) tests, the laboratory should test *Klebsiella pneumoniae* ATCC 700603 (ESBL-producing strain).

NOTE 4: If performing oxacillin salt agar screen tests, the laboratory should test *S. aureus* ATCC 29213 and 43300.

NOTE 5: If performing vancomycin BHI screen tests, the laboratory must test *E. faecalis* 29212 and 51299.

**An equivalent strain is one which demonstrates reactivity similar to an ATCC strain and for which limits have been established. Organisms which manufacturers recommend or require for use in their systems are acceptable strains of control organisms.

Each day the test is performed, the appropriate control strain(s) must be included to check the test system.

When testing is performed daily, for each antimicrobial agent/organism combination, 1 out of every 20 consecutive results may be out of the acceptable range. Any more than 1 out-of-control result in 20 consecutive tests requires corrective action.

Refer to Table 3A*** of the NCCLS Standard, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard-Sixth Edition (M7-A6)" to determine the control strain to be used when performing MIC tests on isolates of Campylobacter jejuni, Haemophilus spp., Neisseria gonorrhoeae, Streptococcus pneumoniae or other organisms as applicable.

EXCEPTION: The laboratory may test each appropriate control strain(s) a minimum of once each test week if the following requirements are met:

The laboratory must document that appropriate control strains are tested for a minimum of 20 or 30 consecutive test days. For each antimicrobial agent/organism combination, no more than one out of 20 or three out of 30 MICs values (i.e., MIC values obtained from one antimicrobial agent/organism combination for 20 or 30 consecutive test days) may be outside established acceptable limits for quality control strains. These limits may be established by the laboratory or the laboratory may use the acceptable range provided in Table 3*** and Table 3A*** of the NCCLS Standard, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard-Sixth Edition (M7-A6)."

NOTE: This procedure is to be used only for demonstrating satisfactory performance for conversion from daily to weekly quality control testing of the MIC test.

After a laboratory has implemented weekly quality control testing of the MIC test:

- Quality control testing must be performed whenever any reagent component of the test is changed (i.e., a new lot of broth from the same manufacturer);
- Corrective action is required if any of the weekly quality control results is outside of the established acceptable range;
- If a new antimicrobial agent is added or a different broth manufacturer is used, it must be tested for 20 or 30 consecutive days and have satisfactory performance documented before it can be tested on a weekly schedule; and
- If there is a major change on the method of reading test results, such as conversion from a visual reading of MICs to an instrument reading or conversion in the type of panel used (i.e., changing from breakpoint to MIC panels), 20 or 30 days of testing is required.

Whenever an MIC value is observed outside the established acceptable limits for quality control strains during weekly quality control testing, the following corrective actions are required:

- If there is an obvious reason for the out-of-control result (e.g., use of the wrong control strain, obvious contamination of the strain or the medium, inadvertent use of the wrong incubation conditions), document the reason and retest the strain on the day the error is observed. If the repeat result is within range, no further corrective action is necessary.
- If there is not an obvious reason for the out-of-control result, test the implicated antimicrobial agent/organism combination on the day the error is observed and test for a total of five (5) consecutive test days. If all 5 MICs for the antimicrobial agent/organism combination are within the established acceptable range, no additional corrective action is necessary.

For the last item mentioned above, if any of the 5 MICs is outside the established acceptable range, additional corrective action is necessary. Daily control of tests must be continued until final resolution of the problem is achieved. Once the problem is corrected, in order to return to weekly quality control testing, documentation of satisfactory performance for another 20 or 30 consecutive days is required.

NCCLS does not address performance issues or make recommendations about any commercial test system such as the E-test. The E-test is a quantitative technique test that determines antimicrobial susceptibility by using a predefined antibiotic gradient to determine the MIC of an individual antibiotic when tested on agar media by overnight incubation. Laboratories using the E-test should rely on the manufacturer to establish the appropriate accuracy control limits and may go to weekly quality control testing after meeting the requirements mentioned in the exception for the procedure to be used for demonstrating satisfactory performance for conversion from daily to weekly quality control testing of the MIC test.

****Permission to use portions of NCCLS publications M2-A8 (Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard-Eighth Edition), and M7-A6 (Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-Sixth Edition), has been granted by NCCLS. Permission to reproduce additional copies or otherwise use the text of M2-A8, and M7-A6 to an extent not permitted under applicable Copyright Law must be obtained from NCCLS by written request. The quality control limits and the interpretive breakpoint tables for the M2-A8 and M7-A6 standards are related and are valid only if the methodology in these standards is used. NCCLS frequently updates the tables through new editions of the standards and supplements. Users should have the most recent editions. The current standards may be obtained from NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087; 610.688.0100, www.nccls.org.*

Table 3. Acceptable Limits for Quality Control Strains Used to Monitor Accuracy of Disk Diffusion Testing of Nonfastidious Organisms (Using Mueller-Hinton Medium Without Blood or Other Supplements)

Antimicrobial Agent	Disk Content	<i>Escherichia coli</i> ATCC® 25922 ^b	<i>Staphylococcus aureus</i> ATCC® 25923	<i>Pseudomonas aeruginosa</i> ATCC® 27853	<i>Escherichia coli</i> ATCC® 35218 ^f
Amikacin	30 µg	19–26	20–26	18–26	–
Amoxicillin-clavulanic acid	20/10 µg	18–24	28–36	–	17–22
Ampicillin	10 µg	16–22	27–35	–	6
Ampicillin-sulbactam	10/10 µg	19–24	29–37	–	13–19
Azithromycin	15 µg	–	21–26	–	–
Azlocillin	75 µg	–	–	24–30	–
Aztreonam	30 µg	28–36	–	23–29	–
Carbenicillin	100 µg	23–29	–	18–24	–
Cefaclor	30 µg	23–27	27–31	–	–
Cefamandole	30 µg	26–32	26–34	–	–
Cefazolin	30 µg	21–27	29–35	–	–
Cefdinir	5 µg	24–28	25–32	–	–
Cefditoren	5 µg	22–28	20–28	–	–
Cefepime	30 µg	31–37	23–29	24–30	–
Cefetamet	10 µg	24–29	–	–	–
Cefixime	5 µg	23–27	–	–	–
Cefmetazole	30 µg	26–32	25–34	–	–
Cefonicid	30 µg	25–29	22–28	–	–
Cefoperazone	75 µg	28–34	24–33	23–29	–
Cefotaxime	30 µg	29–35	25–31	18–22	–
Cefotetan	30 µg	28–34	17–23	–	–
Cefoxitin	30 µg	23–29	23–29	–	–
Cefpodoxime	10 µg	23–28	19–25	–	–
Cefprozil	30 µg	21–27	27–33	–	–
Ceftazidime	30 µg	25–32	16–20	22–29	–
Ceftibuten	30 µg	27–35	–	–	–
Ceftizoxime	30 µg	30–36	27–35	12–17	–
Ceftriaxone	30 µg	29–35	22–28	17–23	–
Cefuroxime	30 µg	20–26	27–35	–	–
Cephalothin	30 µg	15–21	29–37	–	–
Chloramphenicol	30 µg	21–27	19–26	–	–
Cinoxacin	100 µg	26–32	–	–	–
Ciprofloxacin	5 µg	30–40	22–30	25–33	–
Clarithromycin	15 µg	–	26–32	–	–
Clinafloxacin	5 µg	31–40	28–37	27–35	–
Clindamycin	2 µg	–	24–30	–	–
Daptomycin ^d	30 µg	–	18–23	–	–
Dirithromycin	15 µg	–	18–26	–	–
Doxycycline	30 µg	18–24	23–29	–	–
Enoxacin	10 µg	28–36	22–28	22–28	–
Ertapenem	10 µg	29–36	24–31	13–21	–
Erythromycin	15 µg	–	22–30	–	–
Fleroxacin	5 µg	28–34	21–27	12–20	–
Fosfomycin ^c	200 µg	22–30	25–33	–	–
Garenoxacin	5 µg	28–35	30–36	19–25	–
Gatifloxacin	5 µg	30–37	27–33	20–28	–
Gemifloxacin	5 µg	29–36	27–33	19–25	–
Gentamicin ^a	10 µg	19–26	19–27	16–21	–
Grepafloxacin	5 µg	28–36	26–31	20–27	–
Imipenem	10 µg	26–32	–	20–28	–
Kanamycin	30 µg	17–25	19–26	–	–
Levofloxacin	5 µg	29–37	25–30	19–26	–
Linezolid	30 µg	–	25–32	–	–
Lomefloxacin	10 µg	27–33	23–29	22–28	–
Loracarbef	30 µg	23–29	23–31	–	–
Mecillinam	10 µg	24–30	–	–	–

Table 3. (Continued)

Antimicrobial Agent	Disk Content	<i>Escherichia coli</i> ATCC® 25922 ^b	<i>Staphylococcus aureus</i> ATCC® 25923	<i>Pseudomonas aeruginosa</i> ATCC® 27853	<i>Escherichia coli</i> ATCC® 35218 ^f
Meropenem	10 µg	28–34	29–37	27–33	–
Methicillin	5 µg	–	17–22	–	–
Mezlocillin	75 µg	23–29	–	19–25	–
Minocycline	30 µg	19–25	25–30	–	–
Moxalactam	30 µg	28–35	18–24	17–25	–
Moxifloxacin	5 µg	28–35	28–35	17–25	–
Nafcillin	1 µg	–	16–22	–	–
Nalidixic acid	30 µg	22–28	–	–	–
Netilmicin	30 µg	22–30	22–31	17–23	–
Nitrofurantoin	300 µg	20–25	18–22	–	–
Norfloxacin	10 µg	28–35	17–28	22–29	–
Ofloxacin	5 µg	29–33	24–28	17–21	–
Oxacillin	1 µg	–	18–24	–	–
Penicillin	10 units	–	26–37	–	–
Piperacillin	100 µg	24–30	–	25–33	12–18
Piperacillin-tazobactam	100/10 µg	24–30	27–36	25–33	24–30
Quinupristin-dalfopristin	15 µg	–	21–28	–	–
Rifampin	5 µg	8–10	26–34	–	–
Sparfloxacin	5 µg	30–38	27–33	21–29	–
Streptomycin ^a	10 µg	12–20	14–22	–	–
Sulfisoxazole ^e	250 µg or 300 µg	15–23	24–34	–	–
Teicoplanin	30 µg	–	15–21	–	–
Telithromycin	15 µg	–	24–30	–	–
Tetracycline	30 µg	18–25	24–30	–	–
Ticarcillin	75 µg	24–30	–	21–27	6
Ticarcillin-clavulanic acid	75/10 µg	24–30	29–37	20–28	21–25
Tobramycin	10 µg	18–26	19–29	19–25	–
Trimethoprim ^e	5 µg	21–28	19–26	–	–
Trimethoprim-sulfamethoxazole ^e	1.25/23.75 µg	23–29	24–32	–	–
Trospectomycin	30 µg	10–16	15–20	–	–
Trovafoxacin	10 µg	29–36	29–35	21–27	–
Vancomycin	30 µg	–	17–21	–	–

NOTE: Information in boldface type is considered tentative for one year.

Footnotes

- For control limits of gentamicin 120-µg and streptomycin 300-µg disks, use *Enterococcus faecalis* ATCC® 29212 (gentamicin: 16 to 23 mm; streptomycin: 14 to 20 mm).
- ATCC is a registered trademark of the American Type Culture Collection.
- The 200-µg fosfomycin disk contains 50 µg of glucose-6-phosphate.
- Some lots of Mueller-Hinton agar are deficient in calcium and give small zones.
- These agents can be affected by excess levels of thymidine and thymine. See M2, Section 4.1.4 for guidance should a problem with quality control occur.
- Careful organism maintenance is required; refer to M2, Section 10.3.

Table 3A. Acceptable Limits for Quality Control Strains Used to Monitor Accuracy of Disk Diffusion Testing of Fastidious Organisms

Antimicrobial Agent	Disk Content	<i>Haemophilus influenzae</i> ATCC® 49247 ^a	<i>Haemophilus influenzae</i> ATCC® 49766	<i>Neisseria gonorrhoeae</i> ATCC® 49226	<i>Streptococcus pneumoniae</i> ATCC® 49619 ^b
Amoxicillin-clavulanic acid	20/10 µg	15–23	–	–	–
Ampicillin	10 µg	13–21	–	–	30–36
Ampicillin-sulbactam	10/10 µg	14–22	–	–	–
Azithromycin	15 µg	13–21	–	–	19–25
Aztreonam	30 µg	30–38	–	–	–
Cefaclor	30 µg	–	25–31	–	24–32
Cefdinir	5 µg	–	24–31	40–49	26–31
Cefditoren	5 µg	25–34	–	–	27–35
Cefepime	30 µg	25–31	–	37–46	28–35
Cefetamet	10 µg	23–28	–	35–43	–
Cefixime	5 µg	25–33	–	37–45	16–23
Cefmetazole	30 µg	16–21	–	31–36	–
Cefonicid	30 µg	–	30–38	–	–
Cefotaxime	30 µg	31–39	–	38–48	31–39
Cefotetan	30 µg	–	–	30–36	–
Cefoxitin	30 µg	–	–	33–41	–
Cefpodoxime	10 µg	25–31	–	35–43	28–34
Cefprozil	30 µg	–	20–27	–	25–32
Ceftazidime	30 µg	27–35	–	35–43	–
Ceftibuten	30 µg	29–36	–	–	–
Ceftizoxime	30 µg	29–39	–	42–51	28–34
Ceftriaxone	30 µg	31–39	–	39–51	30–35
Cefuroxime	30 µg	–	28–36	33–41	–
Cephalothin	30 µg	–	–	–	26–32
Chloramphenicol	30 µg	31–40	–	–	23–27
Ciprofloxacin	5 µg	34–42	–	48–58	–
Clarithromycin	15 µg	11–17	–	–	25–31
Clinafloxacin	5 µg	34–43	–	–	27–34
Clindamycin	2 µg	–	–	–	19–25
Daptomycin ^c	30 µg	–	–	–	19–26
Dirithromycin	15 µg	–	–	–	18–25
Enoxacin	10 µg	–	–	43–51	–
Ertapenem	10 µg	20–28	27–33	–	28–35
Erythromycin	15 µg	–	–	–	25–30
Fleroxacin	5 µg	30–38	–	43–51	–
Garenoxacin	5 µg	33–41	–	–	26–33
Gatifloxacin	5 µg	33–41	–	45–56	24–31
Gemifloxacin	5 µg	30–37	–	–	28–34
Grepafoxacin	5 µg	32–39	–	44–52	21–28
Imipenem	10 µg	21–29	–	–	–
Levofloxacin	5 µg	32–40	–	–	20–25
Linezolid	30 µg	–	–	–	25–34
Lomefloxacin	10 µg	33–41	–	45–54	–
Loracarbef	30 µg	–	26–32	–	22–28
Meropenem	10 µg	20–28	–	–	28–35
Moxifloxacin	5 µg	31–39	–	–	25–31
Nitrofurantoin	300 µg	–	–	–	23–29
Norfloxacin	10 µg	–	–	–	15–21
Ofloxacin	5 µg	31–40	–	43–51	16–21
Oxacillin	1 µg	–	–	–	≤ 12 ^d
Penicillin	10 units	–	–	26–34	24–30
Piperacillin-tazobactam	100/10 µg	33–38	–	–	–
Quinupristin-dalfopristin	15 µg	15–21	–	–	19–24
Rifampin	5 µg	22–30	–	–	25–30

Table 3A. (Continued)

Antimicrobial Agent	Disk Content	<i>Haemophilus influenzae</i> ATCC® 49247 ^a	<i>Haemophilus influenzae</i> ATCC® 49766	<i>Neisseria gonorrhoeae</i> ATCC® 49226	<i>Streptococcus pneumoniae</i> ATCC® 49619 ^b
Sparfloxacin	5 µg	32–40	–	43–51	21–27
Spectinomycin	100 µg	–	–	23–29	–
Telithromycin	15 µg	17–23	–	–	27–33
Tetracycline	30 µg	14–22	–	30–42	27–31
Trimethoprim-sulfamethoxazole	1.25/23.75 µg	24–32	–	–	20–28
Trospectomycin	30 µg	22–29	–	28–35	–
Trovafloxacin	10 µg	32–39	–	42–55	25–32
Vancomycin	30 µg	–	–	–	20–27

Disk Diffusion Testing Conditions for Clinical Isolates and Performance of Quality Control

Organism	<i>Haemophilus influenzae</i>	<i>Neisseria gonorrhoeae</i>	<i>Streptococcus pneumoniae</i>
Medium	<i>Haemophilus Test Medium</i>	<i>GC agar base and 1% defined growth supplement. The use of a cysteine-free growth supplement is not required for disk diffusion testing.</i>	<i>MHA supplemented with 5% defibrinated sheep blood</i>
Inoculum	<i>Direct colony suspension</i>	<i>Direct colony suspension</i>	<i>Direct colony suspension</i>
Incubation Characteristics	<i>5% CO₂; 16-18 hours; 35 °C</i>	<i>5% CO₂; 20-24 hours; 35 °C</i>	<i>5% CO₂; 20-24 hours; 35 °C</i>

NOTE: Information in boldface is considered tentative for one year.

Footnotes

- a. ATCC is a registered trademark of American Type Culture Collection.
- b. Despite the lack of reliable disk diffusion interpretive criteria for *S. pneumoniae* with certain β -lactams, *Streptococcus pneumoniae* ATCC® 49619 is the strain designated for quality control of all disk diffusion tests with all *Streptococcus spp.*
- c. Some lots of Mueller-Hinton agar are deficient in calcium and give small zones.
- d. Deterioration in oxacillin disk content is best assessed with QC organism *Staphylococcus aureus* ATCC® 25923, with an acceptable zone diameter of 18 to 24 mm.

Table 3. Acceptable Limits for Quality Control Strains Used to Monitor Accuracy of Minimal Inhibitory Concentrations (MICs) ($\mu\text{g/mL}$) of Nonfastidious Organisms (Using Mueller-Hinton Medium Without Blood or Other Supplements)

Antimicrobial Agent	<i>Staphylococcus aureus</i> ATCC® 29213 ^a	<i>Enterococcus faecalis</i> ATCC® 29212	<i>Escherichia coli</i> ATCC® 25922	<i>Pseudomonas aeruginosa</i> ATCC® 27853	<i>Escherichia coli</i> ATCC® 35218 ^b
Amikacin	1–4	64–256	0.5–4	1–4	–
Amoxicillin-clavulanic acid	0.12/0.06–0.5/0.25	0.25/0.12–1.0/0.5	2/1–8/4	–	4/2–16/8
Ampicillin	0.5–2	0.5–2	2–8	–	–
Ampicillin-sulbactam	–	–	2/1–8/4	–	8/4–32/16
Azithromycin	0.5–2	–	–	–	–
Azlocillin	2–8	1–4	8–32	2–8	–
Aztreonam	–	–	0.06–0.25	2–8	–
Carbenicillin	2–8	16–64	4–16	16–64	–
Cefaclor	1–4	–	1–4	–	–
Cefamandole	0.25–1	–	0.25–1	–	–
Cefazolin	0.25–1	–	1–4	–	–
Cefdinir	0.12–0.5	–	0.12–0.5	–	–
Cefditoren	0.25–2	–	0.12–1	–	–
Cefepime	1–4	–	0.016–0.12	1–8	–
Cefetamet	–	–	0.25–1	–	–
Cefixime	8–32	–	0.25–1	–	–
Cefmetazole	0.5–2	–	0.25–2	> 32	–
Cefonicid	1–4	–	0.25–1	–	–
Cefoperazone	1–4	–	0.12–0.5	2–8	–
Cefotaxime	1–4	–	0.03–0.12	8–32	–
Cefotetan	4–16	–	0.06–0.25	–	–
Cefoxitin	1–4	–	2–8	–	–
Cefpodoxime	1–8	–	0.25–1	–	–
Cefprozil	0.25–1	–	1–4	–	–
Ceftazidime	4–16	–	0.06–0.5	1–4	–
Ceftibuten	–	–	0.12–0.5	–	–
Ceftizoxime	2–8	–	0.03–0.12	16–64	–
Ceftriaxone	1–8	–	0.03–0.12	8–64	–
Cefuroxime	0.5–2	–	2–8	–	–
Cephalothin	0.12–0.5	–	4–16	–	–
Chloramphenicol	2–8	4–16	2–8	–	–
Cinoxacin	–	–	2–8	–	–
Ciprofloxacin	0.12–0.5	0.25–2	0.004–0.016	0.25–1	–
Clarithromycin	0.12–0.5	–	–	–	–
Clinafloxacin	0.008–0.06	0.03–0.25	0.002–0.016	0.06–0.5	–
Clindamycin	0.06–0.25	4–16	–	–	–
Daptomycin ^c	0.25–1	1–8	–	–	–
Dirithromycin	1–4	–	–	–	–
Doxycycline	–	–	0.5–2	–	–
Enoxacin	0.5–2	2–16	0.06–0.25	2–8	–
Ertapenem	0.06–0.25	4–16	0.004–0.016	2–8	–
Erythromycin	0.25–1	1–4	–	–	–
Fleroxacin	0.25–1	2–8	0.03–0.12	1–4	–
Fosfomycin ^d	0.5–4	32–128	0.5–2	2–8	–
Garenoxacin	0.004-0.03	0.03-0.25	0.004-0.03	0.5-2	–
Gatifloxacin	0.03–0.12	0.12–1.0	0.008–0.03	0.5–2	–
Gemifloxacin	0.008–0.03	0.016–0.12	0.004–0.016	0.25–1	–
Gentamicin ^e	0.12–1	4–16	0.25–1	0.5–2	–
Grepafloxacin	0.03–0.12	0.12–0.5	0.004–0.03	0.25–2.0	–
Imipenem	0.016–0.06	0.5–2	0.06–0.25	1–4	–
Kanamycin	1–4	16–64	1–4	–	–
Levofloxacin	0.06–0.5	0.25–2	0.008–0.06	0.5–4	–
Linezolid	1–4	1–4	–	–	–

Table 3. (Continued)

Antimicrobial Agent	<i>Staphylococcus aureus</i> ATCC® 29213 ^a	<i>Enterococcus faecalis</i> ATCC® 29212	<i>Escherichia coli</i> ATCC® 25922	<i>Pseudomonas aeruginosa</i> ATCC® 27853	<i>Escherichia coli</i> ATCC® 35218 ^b
Lomefloxacin	0.25–2	2–8	0.03–0.12	1–4	–
Loracarbef	0.5–2	–	0.5–2	>8	–
Mecillinam	–	–	0.03–0.25 ^f	–	–
Meropenem	0.03–0.12	2–8	0.008–0.06	0.25–1	–
Methicillin	0.5–2	>16	–	–	–
Mezlocillin	1–4	1–4	2–8	8–32	–
Minocycline	0.06–0.5	1–4	0.25–1	–	–
Moxalactam	4–16	–	0.12–0.5	8–32	–
Moxifloxacin	0.016–0.12	0.06–0.5	0.008–0.06	1–8	–
Nafcillin	0.12–0.5	2–8	–	–	–
Nalidixic acid	–	–	1–4	–	–
Netilmicin	≤ 0.25	4–16	≤ 0.5–1	0.5–8	–
Nitrofurantoin	8–32	4–16	4–16	–	–
Norfloxacin	0.5–2	2–8	0.03–0.12	1–4	–
Ofloxacin	0.12–1	1–4	0.015–0.12	1–8	–
Oxacillin	0.12–0.5	8–32	–	–	–
Penicillin	0.25–2	1–4	–	–	–
Piperacillin	1–4	1–4	1–4	1–8	–
Piperacillin-tazobactam	0.25/4–2/4	1/4–4/4	1/4–4/4	1/4–8/4	0.5/4–2/4
Quinupristin-dalfopristin	0.25–1	2–8	–	–	–
Rifampin	0.004–0.016	0.5–4	4–16	16–64	–
Sparfloxacin	0.03–0.12	0.12–0.5	0.004–0.016	0.5–2	–
Sulfisoxazole ^g	32–128	32–128	8–32	–	–
Teicoplanin	0.25–1	0.06–0.25	–	–	–
Telithromycin	0.06–0.25	0.016–0.12	–	–	–
Tetracycline	0.12–1	8–32	0.5–2	8–32	–
Ticarcillin	2–8	16–64	4–16	8–32	–
Ticarcillin-clavulanic acid	0.5/2–2/2	16/2–64/2	4/2–16/2	8/2–32/2	8/2–32/2
Tobramycin	0.12–1	8–32	0.25–1	0.25–1	–
Trimethoprim ^g	1–4	≤ 1	0.5–2	>64	–
Trimethoprim-sulfamethoxazole	≤ 0.5/9.5	≤ 0.5/9.5	≤ 0.5/9.5	8/152–32/608	–
Trospectomycin	2–16	2–8	8–32	–	–
Trovafoxacin	0.008–0.03	0.06–0.25	0.004–0.016	0.25–2	–
Vancomycin ^h	0.5–2	1–4	–	–	–

NOTE 1: These MICs were obtained in several reference laboratories by broth microdilution. If four or fewer concentrations are tested, quality control may be more difficult.

NOTE 2: Information in boldface type is considered tentative for one year.

NOTE 3: For four-dilution ranges, results at the extremes of the acceptable range(s) should be suspect. Verify control validity with data from other control strains.

Footnotes

- ATCC is a registered trademark of the American Type Culture Collection.
- Careful organism maintenance is required; refer to M7, Section 12.4.
- QC ranges reflect MICs obtained when Mueller-Hinton broth is supplemented with calcium to a final concentration of 50 µg/mL.
- The approved MIC susceptibility testing method is agar dilution. Agar media should be supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution should not be performed.
- For control organisms for gentamicin and streptomycin high-level aminoglycoside screen tests for enterococci, see Table 2D.
- This test should be performed by agar dilution only.
- Very medium-dependent, especially with enterococci.
- For control organisms for vancomycin screen test for enterococci, see Table 2D.

Table 3A. Acceptable Limits for Quality Control Strains Used to Monitor Accuracy of Minimal Inhibitory Concentrations (MICs) (µg/mL) of Fastidious Organisms

Antimicrobial Agent	<i>Haemophilus influenzae</i> ATCC® 49247 ^a	<i>Haemophilus influenzae</i> ATCC® 49766	<i>Neisseria gonorrhoeae</i> ATCC® 49226	<i>Streptococcus pneumoniae</i> ATCC® 49619	<i>Helicobacter pylori</i> ATCC® 43504	<i>Campylobacter jejuni</i> ATCC® 33560 ^b 36 °C/48 hours	<i>Campylobacter jejuni</i> ATCC® 33560 ^b 42 °C/24 hours
Amoxicillin	–	–	–	0.03–0.12	0.016–0.12	–	–
Amoxicillin-clavulanic	2/1–16/8	–	–	0.03/0.016– 0.12/0.06	–	–	–
Ampicillin	2–8	–	–	0.06–0.25	–	–	–
Ampicillin-sulbactam	2/1–8/4	–	–	–	–	–	–
Azithromycin	1–4	–	–	0.06–0.25	–	–	–
Aztreonam	0.12–0.5	–	–	–	–	–	–
Cefaclor	–	1–4	–	1–4	–	–	–
Cefamandole	–	0.25–1	–	–	–	–	–
Cefdinir	–	0.12–0.5	0.008–0.03	0.03–0.25	–	–	–
Cefditoren	0.06–0.25	–	–	0.016–0.12	–	–	–
Cefepime	0.5–2	–	0.016–0.06	0.03–0.25	–	–	–
Cefetamet	0.5–2	–	0.016–0.25	0.5–2	–	–	–
Cefixime	0.12–1	–	0.004–0.03	–	–	–	–
Cefmetazole	2–16	–	0.5–2	–	–	–	–
Cefonicid	–	0.06–0.25	–	–	–	–	–
Cefotaxime	0.12–0.5	–	0.015–0.06	0.03–0.12	–	–	–
Cefotetan	–	–	0.5–2	–	–	–	–
Cefoxitin	–	–	0.5–2	–	–	–	–
Cefpirome	0.25–1	–	–	–	–	–	–
Cefpodoxime	0.25–1	–	0.03–0.12	0.03–0.12	–	–	–
Cefprozil	–	1–4	–	0.25–1	–	–	–
Ceftazidime	0.12–1	–	0.03–0.12	–	–	–	–
Ceftibuten	0.25–1	–	–	–	–	–	–
Ceftizoxime	0.06–0.5	–	0.008–0.03	0.12–0.5	–	–	–
Ceftriaxone	0.06–0.25	–	0.004–0.016	0.03–0.12	–	–	–
Cefuroxime	–	0.25–1	0.25–1	0.25–1	–	–	–
Cephalothin	–	–	–	0.5–2	–	–	–
Chloramphenicol	0.25–1	–	–	2–8	–	–	–
Ciprofloxacin	0.004–0.03	–	0.001–0.008	–	–	0.12-1	0.06-0.5
Clarithromycin	4–16	–	–	0.03–0.12	0.016–0.12	–	–
Clinafloxacin	0.001–0.008	–	–	0.03–0.12	–	–	–
Clindamycin	–	–	–	0.03–0.12	–	–	–
Daptomycin ^c	–	–	–	0.06–0.5	–	–	–
Dirithromycin	8–32	–	–	0.06–0.25	–	–	–
Doxycycline	–	–	–	–	–	0.5–2	0.25–2
Enoxacin	–	–	0.016–0.06	–	–	–	–
Ertapenem	–	0.016–0.06	–	0.03–0.25	–	–	–
Erythromycin	–	–	–	0.03–0.12	–	1–8	1–4
Fleroxacin	0.03–0.12	–	0.008–0.03	–	–	–	–
Garenoxacin	0.002-0.008	–	–	0.016–0.06	–	–	–
Gatifloxacin	0.004–0.03	–	0.002–0.016	0.12–0.5	–	–	–
Gemifloxacin	0.002–0.008	–	–	0.008–0.03	–	–	–
Gentamicin	–	–	–	–	–	0.5–2	0.5–4
Grepafloxacin	0.002–0.016	–	0.004–0.03	0.06–0.5	–	–	–
Imipenem	–	0.25–1	–	0.03–0.12	–	–	–
Levofloxacin	0.008–0.03	–	–	0.5–2	–	–	–
Linezolid	–	–	–	0.5–2	–	–	–
Lomefloxacin	0.03–0.12	–	0.008–0.03	–	–	–	–
Loracarbef	–	0.5–2	–	2–8	–	–	–
Metronidazole	–	–	–	–	64–256	–	–
Meropenem	–	0.03–0.12	–	0.06–0.25	–	0.004–0.015	0.008–0.03
Moxifloxacin	0.008–0.03	–	–	0.06–0.25	–	–	–

Table 3A. (Continued)

Antimicrobial Agent	<i>Haemophilus influenzae</i> ATCC® 49247 ^a	<i>Haemophilus influenzae</i> ATCC 49766	<i>Neisseria gonorrhoeae</i> ATCC® 49226	<i>Streptococcus pneumoniae</i> ATCC® 49619	<i>Helicobacter pylori</i> ATCC® 43504	<i>Campylobacter jejuni</i> ATCC® 33560 ^b 36 °C/48 hours	<i>Campylobacter jejuni</i> ATCC® 33560 ^b 42 °C/24 hours
Nitrofurantoin	–	–	–	4–16	–	–	–
Norfloxacin	–	–	–	2–8	–	–	–
Ofloxacin	0.016–0.06	–	0.004–0.016	1–4	–	–	–
Penicillin	–	–	0.25–1	0.25–1	–	–	–
Piperacillin-tazobactam	0.06/4–0.5/4	–	–	–	–	–	–
Quinupristin-dalfopristin	2–8	–	–	0.25–1	–	–	–
Rifampin	0.25–1	–	–	0.015–0.06	–	–	–
Sparfloxacin	0.004–0.016	–	0.004–0.016	0.12–0.5	–	–	–
Spectinomycin	–	–	8–32	–	–	–	–
Telithromycin	1–4	–	–	0.004–0.03	0.06–0.5	–	–
Tetracycline	4–32	–	0.25–1	0.12–0.5	0.12–1.0	–	–
Trimethoprim-sulfamethoxazole	0.03/0.59–0.25/4.75	–	–	0.12/2.4–1/19	–	–	–
Trospectomycin	0.5–2	–	1–4	1–4	–	–	–
Trovafoxacin	0.004–0.016	–	0.004–0.016	0.06–0.25	–	–	–
Vancomycin	–	–	–	0.12–0.5	–	–	–

Testing Conditions for Clinical Isolates and Performance of Quality Control

Organism	<i>Haemophilus influenzae</i>	<i>Neisseria gonorrhoeae</i>	<i>Streptococcus pneumoniae</i>	<i>Helicobacter pylori</i>	<i>Campylobacter</i> spp.
Medium	Broth dilution: Haemophilus Test Medium (HTM) broth	Agar dilution: GC agar base and 1% defined growth supplement. The use of a cysteine-free supplement is required for agar dilution tests with carbapenems and clavulanate. Cysteine-containing defined growth supplements <i>do not</i> significantly alter dilution test results with other drugs.	Broth dilution: Cation-adjusted Mueller-Hinton broth with lysed horse blood (2–5% v/v).	Agar Dilution: Mueller-Hinton agar with aged (≥ 2-week-old) sheep blood (5% v/v).	Agar dilution: Mueller-Hinton agar with 5% defibrinated sheep blood
Inoculum	Direct colony suspension, equivalent to a 0.5 McFarland standard	Direct colony suspension, equivalent to a 0.5 McFarland standard	Direct colony suspension, equivalent to a 0.5 McFarland standard	See footnote d, below.	Direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation Characteristics	35 °C; ambient air; 20–24 hours	35 °C; 5% CO ₂ ; 20–24 hours	35 °C; ambient air; 20–24 hours	35 °C; 3 days; microaerobic atmosphere produced by gas-generating system suitable for campylobacters.	36 °C /48 hours or 42 °C/ 24 hours; 10% CO₂, 5% O₂ and 85% N₂ or a microaerophilic environment

NOTE 1: Information in boldface type is considered tentative for one year.

NOTE 2: For four-dilution ranges, results at the extremes of the acceptable range(s) should be suspect. Verify control validity with data from other control strains.

Footnotes

- ATCC is a registered trademark of the American Type Culture Collection.
- Since some isolates of *C. jejuni* ssp. *doylei*, *C. fetus* and *C. lari* may not grow at 42 °C, susceptibility testing of these isolates should be performed at 36 °C.
- QC ranges reflect MICs obtained when Mueller-Hinton broth is supplemented with calcium to a final concentration of 50 µg/mL.
- The inoculum for testing of *Helicobacter pylori* should be as follows: a saline suspension equivalent to a 2.0 McFarland standard (containing 1x10⁷ to 1x10⁸ CFU/mL), to be prepared from a 72-hour-old subculture from a blood agar plate. The inoculum (1 to 3 µL per spot) is replicated directly on the antimicrobial agent-containing agar dilution plates.

§493.1261 Standard: Bacteriology.

(c) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1261(c)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were tested when shipments of reagents, disks, stains, or antisera for identification systems were opened or when the laboratory prepared these materials.

D5511

§493.1262 Standard: Mycobacteriology.

(a) Each day of use, the laboratory must check all reagents or test procedures used for mycobacteria identification with at least one acid-fast organism that produces a positive reaction and an acid-fast organism that produces a negative reaction.

Interpretive Guidelines §493.1262(a)

When condition level deficiencies in Mycobacteriology are in any or all phases of testing, use D5004.

For acid-fast stains (i.e., Ziehl-Neelsen, Kinyoun), use positive and negative stain controls each day of testing patient samples. Use D5473. For fluorochrome acid-fast stains, use positive and negative stain controls each time of use. Use D5475.

Controls for acid-fast and fluorochrome stains for clinical specimens can include previously processed specimens that contain confirmed acid-fast organisms such as Mycobacterium fortuitum or other non-tuberculous mycobacteria for the positive control, and a negative sputum seeded with Escherichia coli for a negative control. Control smears should be heat-fixed and stored in a protective box.

For controls when staining mycobacteriology cultures, use a previously confirmed acid-fast organism for the positive control, and a non-mycobacterial species such as Escherichia coli for the negative control.

For the BACTEC NAP test, positive and negative control organisms must be tested each week of use. Controls should include M. tuberculosis ATCC 27294 and M. kansasii ATCC 35775. M. tuberculosis should be inhibited by NAP, while M. kansasii should have increasing growth index values in the presence of NAP.

For molecular amplification testing guidelines, use D5455.

Probes §493.1262(a)

How often are mycobacteriology cultures checked for growth prior to the issuance of final patient reports? How long are negative cultures held before a final patient report is issued (e.g., minimum of six weeks)? Use D5411 and D5413 as appropriate.

D5513

§493.1262 Standard: Mycobacteriology.

(b) For antimycobacterial susceptibility tests, the laboratory must check each batch of media and each lot number and shipment of antimycobacterial agent(s) before, or concurrent with, initial use, using an appropriate control organism(s).

Interpretive Guidelines §493.1262(b)

A susceptible control strain of Mycobacterium tuberculosis, such as H37Rv or other appropriate control strain, must be used to check the susceptibility procedure.

For automated mycobacterial susceptibility testing, organisms which manufacturers recommend or require for use in their systems are acceptable strains of control organisms.

Probes §493.1262(b)

Are quality control samples tested at the same time specimens are tested? For example, a growth control without antimycobacterial agent should be inoculated at the time of patient testing.

(b)(1) The laboratory must establish limits for acceptable control results.

Probes §493.1262(b)(1)

Which control strains are used and how did the laboratory establish acceptable control limits for susceptibility tests?

(b)(2) Each week tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

(b)(3) The results for the control organism(s) must be within established limits before reporting patient results.

Interpretive Guidelines 493.1262(b)(3)

The laboratory must ensure that it performs and documents all corrective action(s) taken whenever the test results do not meet the laboratory control limits for susceptibility. Use D5781.

§493.1262 Standard: Mycobacteriology.

(c) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1262(c)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were tested when shipments of reagents, disks, stains, or antisera for identification systems were opened or when the laboratory prepared these materials.

D5517

§493.1263 Standard: Mycology.

(a) The laboratory must check each batch (prepared in-house), lot number (commercially prepared), and shipment of lactophenol cotton blue when prepared or opened for intended reactivity with a control organism(s).

Interpretive Guidelines §493.1263(a)

When condition-level deficiencies in Mycology are in any or all phases of testing, use D5006.

For non-culture identification systems (e.g., direct antigen) use D5449 and/or D5453 as appropriate.

A filamentous fungus such as Aspergillus species should be used to check staining of lactophenol cotton blue.

D5519

§493.1263 Standard: Mycology.

(b) For antifungal susceptibility tests, the laboratory must check each batch of media and each lot number and shipment of antifungal agent(s) before, or concurrent with, initial use, using an appropriate control organism(s).

(b)(1) The laboratory must establish limits for acceptable control results.

Probes §493.1263(b)(1)

Which control strains are used and how did the laboratory establish acceptable control limits for susceptibility tests?

(b)(2) Each day tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

Probes §493.1263(b)(2)

Are quality control samples tested at the same time specimens are tested?

(b)(3) The results for the control organism(s) must be within established limits before reporting patient results.

§493.1263 Standard: Mycology.

(c) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1263(c)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were tested when shipments of reagents, discs, stains, or antisera for identification systems were opened or when the laboratory prepared these materials.

D5523

§493.1264 Standard: Parasitology.

(a) The laboratory must have available a reference collection of slides or photographs and, if available, gross specimens for identification of parasites and use these references in the laboratory for appropriate comparison with diagnostic specimens.

Interpretive Guidelines §493.1264(a)

When condition level deficiencies in Parasitology are in any or all phases of testing, use D5008.

The laboratory must have adequate reference material, but does not have to maintain several different reference systems. Textbooks with photographs, previously stained slide preparations, preserved specimens, or slides from proficiency testing programs are some acceptable systems.

If the laboratory uses zinc sulfate for concentration of fecal specimens for ova and parasite examinations, the acceptable specific gravity of the zinc sulfate solution is 1.18 for fresh fecal samples and 1.20 for formalinized fecal samples. Use D3007 or D5411 as applicable.

For non-culture identification systems (e.g., direct antigen) use D5449 and/or D5453 as appropriate.

D5525

§493.1264 Standard: Parasitology.

(b) The laboratory must calibrate and use the calibrated ocular micrometer for determining the size of ova and parasites, if size is a critical parameter.

Interpretive Guidelines §493.1264(b)

Check for the following:

- *Presence of an ocular micrometer for the microscope(s) used;*
- *Availability of a stage micrometer;*
- *Instructions for calibration. Use D5403;*
- *Records of the measurements and calculations used to show that each objective (high, oil, low) has been calibrated; and*
- *Criteria for the use of the micrometer for determining the size of ova and parasites. Use D5403.*

Probes §493.1264(b)

How has the laboratory determined the accuracy of the ocular calibration and that the staff has the knowledge for proper use?

D5527

§493.1264 Standard: Parasitology.

(c) Each month of use, the laboratory must check permanent stains using a fecal sample control material that will demonstrate staining characteristics.

Interpretive Guidelines §493.1264(c)

The fecal sample control may contain either parasites or added leukocytes sufficient to demonstrate staining characteristics. A commercially prepared quality control slide for intestinal parasites is also an acceptable control for checking permanent stains.

While a wet mount preparation may not be sufficiently sensitive to detect small numbers of ova or parasites in fecal specimens, or to render a final species identification, the regulations do not require use of concentrated and permanent stain techniques to identify fecal parasites. It is the laboratory's responsibility to assure that it can accurately and reliably identify the organisms it claims to be able to identify. Use D3007 and/or D5411

as applicable. Upon request, the laboratory must specify the method employed by the laboratory for screening fecal specimens and provide information to clients on the test report that may affect the interpretation of test results. Use D5805 and/or D5809 as applicable.

The working iodine solution is stable for approximately two weeks. If the laboratory does not prepare fresh working iodine solution at least every two weeks, it must assure that the iodine solution has not deteriorated by observing positive clinical specimens or formalin-fixed specimens. Use D5417. Protozoan cysts stained with iodine contain golden yellow cytoplasm, brown glycogen material and have refractile nuclei.

§493.1264 Standard: Parasitology.

(d) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1264(d)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were tested when shipments of reagents, disks, stains, or antisera for identification systems were opened or when the laboratory prepared these materials. QC records should also include documentation of the measurements and calculations for calibration of each objective (low, high, oil immersion) of the ocular micrometer, and demonstrate that permanent stain controls were tested with a fecal sample control material each month of use.

D5531

§493.1265 Standard: Virology.

(a) When using cell culture to isolate or identify viruses, the laboratory must simultaneously incubate a cell substrate control or uninoculated cells as a negative control material.

Interpretive Guidelines §493.1265(a)

When condition level deficiencies in Virology are in any or all phases of testing, use D5010.

Cell Culture

For commercially purchased cell culture media, the requirement for media quality control checks is satisfied by visually examining the media for sterility and assuring the ability of the media to sustain cell life. If the media is prepared or produced in the laboratory, use D5477:

- Each component of cell culture media should be checked for sterility using bacterial culture techniques. In addition, fetal bovine serum must be checked for toxicity using cell culture systems;
- The combined product (e.g., Hanks, Eagles and Earles) should be checked for sterility using bacterial culture techniques and the ability to propagate growth with cell cultures; and
- Cell culture systems should be checked for mycoplasma contamination at regular intervals established by the laboratory.

Non-culture Methods

1. For other non-culture identification (e.g., antigen identification) systems that are used for viral identification, the laboratory is not required to maintain live viral cultures for quality control purposes. However, positive and negative controls are required to evaluate the detection phase, if such controls are available commercially or in the laboratory. Use D5449 and/or D5453 as appropriate.
2. If organism controls are not available, a previously extracted viral antigen as the positive control plus a previously confirmed negative control of the same matrix as the patient sample may be used. Use D5485. A positive organism control must be subjected to the extraction process if such a control is available in the laboratory. Use D5453.
3. For fluorescent stains, the control requirements are met by using virus-infected cells for a positive control among uninfected cells for a negative control. Use D5475.

The intent of the regulations is for the laboratory to have methodologies available to isolate and identify the viruses that are etiologically related to the clinical disease for which services are offered. For example, if a laboratory offers services only for Herpes testing, it must have available host systems for the isolation and/or test methods for the identification of the Herpes virus. If the laboratory is not using the appropriate host system, use D3007.

"Host system" is defined as the animal, egg or cell culture model, which supports the propagation of viruses.

Clinical information important for the determination and selection of the proper host system should include (Use D5305):

- Clinical symptoms of the patient;
- Age of the patient;
- Source of the specimen;
- Date of onset of clinical symptoms;
- Recent travel information of patient;
- Test request; and
- Date of specimen collection.

Cell culture is the host system used most frequently. The specific cell line (type) is usually selected based upon its known sensitivity and susceptibility to different viruses. For example, the cell lines to be used as host systems for the following clinical specimens could be:

- Upper respiratory infection specimens: Primary Monkey Kidney (PMK), Human Fetal Diploid Lung (HFDL), or equivalent;
- Enteric specimens: PMK, Human Fetal Diploid Kidney (HFDK), or equivalent;
- Urine specimens: HFDL, PMK, or equivalent;
- Genital specimens: Human Foreskin (HFD), Vero (Continuous Monkey Kidney), or equivalent;
- Vesicular lesions: HFDL, PMK, BSC-1 (Monkey Cell Line), or equivalent; and
- Tissues or Spinal fluids: PMK, Vero, BSC-1, HFDK or HFDL, or equivalent.

Prior to the inoculation of the cell cultures, the laboratory should check the cell culture systems for the following:

- The age of the cell culture monolayer (no more than 7-10 days post "seeding") (Use D5417);
- Maintenance media that is free from inhibitory substances (Use D5477); and
- Sterility (visual observation for turbidity) (Use D5477).

Uninoculated cell substrate controls are used to determine whether the specificity of a test system has been assured. Generally, an uninoculated cell control for each cell line that is inoculated is used per inoculation day to determine whether the consequent cytopathic effect (CPE) in the cells inoculated with patient specimen was caused by specific etiologic agent(s), or caused by the nonspecific deterioration of the cells themselves. Often, as monolayer host cells age, the cells deteriorate, exhibiting "rounding" and "pulling-apart." This cell change may be confused with CPE if uninoculated cells are not available to compare with the inoculated cells.

Probes §493.1265(a)

How does the laboratory determine the specific cell line to be used as the host system? Use D3007 or D5411 as applicable.

When reviewing the laboratory's identification procedures for the clinical diseases for which services are offered, how does the laboratory rule out the presence of Clostridium difficile toxin in those cell cultures in which the patient specimen exhibits non-specific effects unrelated to viral cytopathic effect (CPE)? Use D3007 or D5411 as applicable.

If presumptive reports are issued based on CPE, how does the laboratory confirm the identification reported? Use D3007 or D5411 as applicable.

For tests such as hemagglutination inhibition and viral neutralization in which antisera must be standardized, how has the laboratory determined the optimum dilution of the antisera to assure maximum sensitivity and specificity? Use D5437.

Neutralization Tests:

How does the laboratory standardize its dilution of the viral isolate and control virus to the appropriate Tissue Culture Dose 50 or equivalent, each time the test is performed? Use D5437.

How many varieties of uninoculated cell cultures does the laboratory use to check each new lot of anti-serum or serum pool for toxicity? Use D5477 or 5479 as applicable.

Hemagglutination Inhibition Tests:

After having determined the hemagglutination titer, how does the laboratory determine the working dilution of the viral isolate (i.e., usually 4 Hemagglutination units)? How does the laboratory ensure that this working dilution is correct for isolates and controls? Use D5421 or D5423 as applicable.

How often and for which hemagglutination inhibition tests does the laboratory include a serum/cell/buffer control and a cell/buffer control? Use D5425.

Does the laboratory include one known virus or viral antigen specific to each antisera used in the test procedure? Use D5449.

Direct Immunofluorescence Tests:

How does the laboratory determine which immune serum conjugate(s) to use when identifying viruses using antisera that react with viruses that are etiologically similar (e.g., an antigen test for specimens from patients with flu-like symptoms that identifies Respiratory Syncytial Virus, Influenza, and Parainfluenza)? How does the laboratory assure the specificity of this conjugate for the specific virus being identified? Use D5421 or D5423 as applicable.

How does the laboratory rule out non-specific reactivity for each conjugate used? Use D5421 or D5423 as applicable.

Indirect Immunofluorescence Tests:

Has the laboratory determined the optimum dilution of its anti-species [e.g., antibody to host system or cell culture (such as anti-PMK, conjugated immune serum)]? Use D5421 or D5423 as applicable.

Has the laboratory determined the optimum dilution of the virus specific immune serum? Use D5421 or D5423 as applicable.

Determine whether the laboratory is checking positive and negative reactivity using (Use D5475.):

- Uninoculated cells plus immune serum plus anti-species conjugate (negative control); and
- Viral antigen or known virus infected cells plus immune serum plus anti-species conjugate (positive control).

Determine whether the laboratory checks each new batch or shipment of conjugate using known virus infected cells plus PBS plus anti-species conjugate. Use D5471.

§493.1265 Standard: Virology.

(b) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1265(b)

QC records must identify the host cell cultures employed, the number of tubes or plates inoculated or uninoculated, maintenance medium used, the number of times the patient specimen was sub-cultured, the specific sub-culture or passage in which the virus was identified, the CPE observed, and post inoculation date of observations. If the deficiency is due to absence of dates of testing and observations, use D5787.

§493.1267 Standard: Routine chemistry.

For blood gas analyses, the laboratory must perform the following:

Interpretive Guidelines §493.1267(a)-(d):

When condition level deficiencies in Routine Chemistry are identified in one or more phases of testing, use D5016.

Control materials generally are not available to verify the reportable range at the very high range of patient results. When necessary, the laboratory may verify the results by splitting patient samples and assaying them on two different blood gas analyzers.

Quality control records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reaction and/or observations and demonstrate that controls were tested as required.

Do not dictate the acceptable format for documentation.

Probes §493.1267(a)-(d):

For blood gas testing, do the records include barometric pressure and room temperature, as necessary?

Do the records of a laboratory that moves from testing site to testing site demonstrate the

performance of control samples following transport of equipment when such activity affects test performance specifications and/or instrument calibration?

D5535

§493.1267 Standard: Routine chemistry.

(a) Calibrate or verify calibration according to the manufacturer's specifications and with at least the frequency recommended by the manufacturer.

Interpretive Guidelines §493.1267(a)

For blood gas analysis, the laboratory must perform calibration and calibration verification in accordance with the manufacturer's instructions. If the laboratory meets the manufacturer's instructions, and the requirements at this section, the laboratory does not have to adhere to calibration and calibration verification requirements at §493.1255.

D5537

§493.1267 Standard: Routine chemistry.

(b) Test one sample of control material each 8 hours of testing using a combination of control materials that include both low and high values on each day of testing.

Interpretive Guideline§493.1267(b)

"Each 8 Hours of testing" is defined as each shift of 8 consecutive hours the laboratory is in operation, including "on-call" shifts. When documenting standards/controls results, the laboratory must identify the shifts in which controls are tested with patients.

For a laboratory that is only open 8 hours/day and the instrument autocalibrators, the laboratory must test both a low and high value in the eight hours to meet the requirement.

In addition to testing one control each eight hours, the combination of controls and calibrators used each day of testing must include a high and low value. Controls should be rotated to check normal, alkalosis and acidosis levels.

D5539

§493.1267 Standard: Routine chemistry.

(c) Test one sample of control material each time specimens are tested unless automated instrumentation internally verifies calibration at least every 30 minutes.

Interpretive Guidelines §493.1267(c)

If blood gas analysis is performed with an instrument that does not internally verify the calibration at least every thirty minutes, then a calibrator or control must be tested each time patient specimens are tested.

It is not the intent of this requirement to require the laboratory to maintain records of each auto-calibration.

§493.1267 Standard: Routine chemistry.

(d) Document all control procedures performed, as specified in this section.

D5543

§493.1269 Standard: Hematology.

(a) For manual cell counts performed using a hemocytometer--

(a)(1) One control material must be tested each 8 hours of operation; and

(a)(2) Patient specimens and control materials must be tested in duplicate.

Interpretive Guidelines §493.1269(a)

When condition level deficiencies in Hematology are in any or all phases of testing, use D5024.

"Hours of operation" is defined as each shift of 8 consecutive hours the laboratory is in operation, including "on-call" shifts. When documenting standards/controls results, the laboratory must identify the shifts in which controls are tested with patients.

If the manufacturer of an instrument that performs automated differentials does not give criteria for when to perform a manual differential, the laboratory must establish criteria indicating when to perform a manual differential including instructions for reporting the results. Use D5423.

Control requirements for automated instruments that perform hemoglobin, hematocrit, red and white cell counts and differentials are found at §493.1256(d)(3)(i). Use D5447. The calibration verification exception for automated hematology cell counters is found at §493.1255(b). Use D5439.

D5545

§493.1269 Standard: Hematology.

(b) For all nonmanual coagulation test systems, the laboratory must include two levels of control material each 8 hours of operation and each time a reagent is changed.

Interpretive Guidelines §493.1269(b)-(c):

The laboratory performing non-manual coagulation tests subject to §493.1269 must either establish criteria or verify manufacturer's criteria for an acceptable range of performance as required in §493.1253(a). Use D5421 or D5423 as appropriate.

An automated (nonmanual) coagulation test system samples the plasma, combines the plasma with the reagents, detects the end point or clot formation and displays the test results without operator intervention.

The International Sensitivity Index (ISI) is the correction factor for variable sensitivities of thromboplastins. The International Normalized Ratio (INR) is a calculation primarily used for monitoring a patient's oral anticoagulant therapy. The INR corrects for the variability in Prothrombin Time (PT) results attributable to the ISI. Therefore, this allows all PT's to be corrected to the international standard.

INR Calculation

The INR is equal to the ratio of the patient's PT (in seconds) to the laboratory's established normal mean PT (in seconds), then raised to the power of the ISI.

$$\text{INR} = (\text{Patient PT} \div \text{Mean Normal Range PT})^{\text{ISI}}$$

NOTE: A scientific calculator is needed to calculate the INR.

Example:

Patient PT (in seconds)=18.5

Normal mean PT (in seconds)=12.9

ISI value (obtain from the package insert of the laboratory's current lot of thromboplastin reagent)=2.002

1. $18.5 \div 12.9 = 1.434$ (Patient Ratio)
2. $1.434^{2.002} = 2.056$ (INR Result)
3. Report the INR as: INR=2.1.

For INR calculations, ensure that the laboratory:

- Establishes a normal Prothrombin time mean with each new thromboplastin lot number, while testing patients with results in the therapeutic range and abnormal patients with the old lot and the new lot of reagents to verify consistency of results;
- Incorporates the current and pertinent normal Prothrombin time mean and ISI value for each lot of thromboplastin (manual, instrument, or LIS);
- Documents the manual check of the INR calculation for each new lot number; and
- Documents each thromboplastin lot number, with the normal Prothrombin time mean and the ISI value provided by the manufacturer (manual or instrument).

Probes §493.1269(b)-(c):

Is the laboratory using the ISI value from the current manufacturer's package insert in calculating the INR values?

How does the laboratory ensure that the ISI values are changed with each change of thromboplastin lot number?

Has the laboratory established their own normal patient mean with each lot of thromboplastin?

For coagulation testing, do the records include timer checks, and temperature checks as necessary?

D5547

§493.1269 Standard: Hematology.

(c) For manual coagulation tests--

(c)(1) Each individual performing tests must test two levels of control materials before testing patient samples and each time a reagent is changed; and

(c)(2) Patient specimens and control materials must be tested in duplicate.

§493.1269 Standard: Hematology.

(d) The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1269(d)

Quality control records should include lot numbers, date prepared/opened, expiration dates, the actual measurement(s) taken, reactions and/or observations and demonstrate that controls were tested when shipments of reagents or stains were opened or when the laboratory prepared these materials. However, do not dictate the acceptable format for documentation.

D5551

§493.1271 Standard: Immunohematology.

(a) Patient testing.

(a)(1) The laboratory must perform ABO grouping, D(Rho) typing, unexpected antibody detection, antibody identification, and compatibility testing by following the manufacturer's instructions, if provided, and as applicable, 21 CFR 606.151(a) through (e).

Interpretive Guidelines §493.1271(a)(1)

When condition level deficiencies in Immunohematology are in any or all phases of testing, use D5026.

There are no daily quality control requirements for reagent red cell panels used in antibody identification. Panel quality control is a combination of serological test results, such as: strength of reactions and patient phenotype; statistical probability, patient's medical history; and laboratory standard of practice (i.e., how the laboratory handles compatibility testing for patients with unexpected antibodies). However, the QC requirements pertaining to new batch, lot, shipment of identification systems at §493.1256(e)(1) must be met.

The following table defines the frequency and the type of quality control to be performed for each container of antisera and reagent red cells use for immunohematology testing:

<u>Reagent</u>	<u>Positive Control</u>	<u>Negative Control</u>
ABO Antisera	Each day of use	N/A
Rh Antisera	Each day of use	Each day of use
Other Anti-sera	*Each day of use	Each day of use
*Anti-human globulin sera	*Each day of use	*Each day of use
ABO Reagent red cells	Each day of use	N/A
Antibody Screening cells (at least one known antibody)	Each day of use	N/A

In daily quality control testing, it is sufficient to test antiglobulin serum for IgG only. Anticomplement activity can be checked, if desired, against complement coated RBC's but this need not be a routine procedure.

*This requirement is satisfied by checking the antihuman immune globulin (Coombs Serum) in one of the following ways:

- React anti-human globulin with a pre-sensitized reagent red blood cell which is either prepared commercially or by the laboratory;
- Perform the quality control for antibody detection using a known antibody which is demonstrated by the addition of antihuman globulin; or
- Add a pre-sensitized reagent red blood cell to all negative antiglobulin tests (direct antiglobulin, indirect antiglobulin, antibody detection and identification test)

to indicate that antiglobulin serum present in the test was not inactivated by

Interpretive Guidelines §493.1271(a)(1)

unbound globulins or diluted by excess residual saline, and that the negative results reflect true absence of reactivity in the test. Using green antiglobulin serum does not substitute for this control.

Blood banks may make their own reagents. If unlicensed reagents are used, the facility must follow FDA's Current Good Manufacturing Practices (CGMP) and additional standards found at:

- 21 CFR 606.65 (c), (d), (e);
- 21 CFR 606.160 (b)(4), (5), (7);
- 21 CFR 606.160(d);
- 21 CFR 640.5(b), (c);
- and 21 CFR 660 subpart D.

Rare reagents, e.g. anti-Jk^b, and anti-Le^b, etc. are sometimes used beyond the expiration date; this is acceptable only if adequate controls are used and the reactivity and specificity of the reagents are documented.

- Determine the laboratory's policies regarding:
- Compatibility testing for patients with a history of a prior antibody;
- Compatibility testing for patients with no history of a prior antibody;
- Retyping, rescreening, and/or recrossmatching units which are not transfused at the original requested time; and
- Course of action to be taken for positive antibody screening and/or incompatible crossmatch.

For deficiencies relating to director responsibilities use D6082.

For deficiencies relating to step-by-step procedure use D5403.

If the laboratory performs gel techniques for ABO, Rh or Antibody screening, ensure the laboratory maintains the proper centrifuge speed, centrifuge time, and pipet dispensing volume.

Probes §493.1271(a)(1)

If the patient has been previously tested, how are results of current testing compared with interpretations of previous testing? When the results of current testing are discrepant with results of previous testing, how has the laboratory resolved the difference? Use D5757.

§493.1271 Standard: Immunohematology.

(a)(2) The laboratory must determine ABO group by concurrently testing unknown red cells with, at a minimum, anti-A and anti-B grouping reagents. For confirmation of ABO group, the unknown serum must be tested with known A1 and B red cells.

Interpretive Guidelines §493.1271(a)(2)

Determine if the laboratory has a policy to detect and resolve ABO discrepancies. If the laboratory does not have such procedures, use D5401. If the laboratory does not use patient records to confirm ABO group (i.e., current testing compared with historical records when available), use D5751.

§493.1271 Standard: Immunohematology.

(a)(3) The laboratory must determine the D(Rho) type by testing unknown red cells with anti-D (anti-Rho) blood typing reagent.

Interpretive Guidelines §493.1271(a)(3)

Determine if the laboratory has established a policy specifying when testing for weak D (Du) must be performed.

Probes §493.1271(a)(3)

Is the laboratory following this policy?

D5553

§493.1271 Standard: Immunohematology.

(b) Immunohematological testing and distribution of blood and blood products. Blood and blood product testing and distribution must comply with 21 CFR 606.100(b)(12); 606.160(b)(3)(ii) and (b)(3)(v); 610.40; 640.5(a); 640.5(b); 640.5(c); 640.5(e); and 640.11(b).

Interpretive Guidelines §493.1271(b)

NOTE: The focus of the FDA is on the manufacture of a safe and efficacious blood and blood product for transfusion and further manufacture, and on maintaining a healthy donor population. CLIA does not apply to quality control testing performed on specimens from the blood or blood products (e.g. pH, platelet count, hemolysis, volume). CLIA is concerned with the health of the individual donating, and the recipient of the blood product. CLIA is applicable to all testing performed in a donor situation because it is assessing the health of the donor or whether there is a potential for harm to the recipient if performed incorrectly (e.g., ABO, RH, antibody screen, HIV, Hepatitis, RPR, total protein, drug testing).

Refer to the current version of 21 CFR Parts 600-799 for the specified sections:

- §606.100(b)(12) - Criteria for determining whether returned blood is suitable for reissue;
- §606.160(b)(3)(ii) – Visual inspection of whole blood and red blood cells during storage and immediately before distribution;
- §606.160(b)(3)(v) – Emergency release of blood, including signature of requesting physician obtained before or after release;
- §610.40 Testing for communicable diseases;
- §640.5(a) Syphilis testing;
- §640.5(b) Determination of Blood group;

Interpretive Guidelines §493.1271(b)

- §640.5(c) Determination of Rh factor;
- §640.5(e) Inspection of whole blood during storage and immediately prior to issue; and
- §640.11(b) Inspection of RBC during storage and at the time of issue.

Probes §493.1271

If equipment and reagents are used in mobile or temporary testing sites, how are they protected from extreme temperature fluctuations when not in use (e.g., evenings, weekends, and holidays)?

D5555

§493.1271 Standard: Immunohematology.

(c) Blood and blood products storage. Blood and blood products must be stored under appropriate conditions that include an adequate temperature alarm system that is regularly inspected.

(c)(1) An audible alarm system must monitor proper blood and blood product storage temperature over a 24-hour period.

(c)(2) Inspections of the alarm system must be documented.

Interpretive Guidelines §493.1271(c)

Acceptable temperature ranges must be established and actual readings of temperature-controlled storage areas must be recorded during the time that blood or blood products for transfusion are stored. Whole Blood, Red Blood Cells, and Liquid Plasma should be stored between 1 and 6°C; room temperature Platelets and Platelet Rich Plasma between 20 and 24°C or 1-6°C as indicated on the product label. Fresh Frozen Plasma, Plasma, and Cryoprecipitated AHF should be stored at -18°C or colder. Temperatures continuously monitored by a recording thermograph or central monitoring system are acceptable. The charts or central monitoring system must be retained to document that temperatures are maintained within the FDA's acceptable limits.

Verify that the laboratory regularly inspects the alarm system(s) according to its established policy. When the facility performs alarm checks, the temperature at which the alarm sounds should be compared to the temperature on the recording chart. Verify that the alarm activates at the appropriate temperature(s).

FDA Reissue requirements are as follows: The container must have a tamper-proof seal which remains unbroken; and tamper-proof pilot tube or segment must be attached; records should indicate that the blood was maintained at 1 - 10°C while outside the control of the establishment; and the unit must be inspected prior to reissue. Blood issued for transfusion to a ward or operating room and not refrigerated may be reissued if the unit is returned to the blood bank within 30 minutes.

Probes §493.1271(c)

Does the laboratory ensure that the freezer(s) used to store blood products is maintained at the recommended temperature(s) on a continuous basis?

Does the laboratory document and explain unacceptable storage temperatures? Use D5793.

What is the laboratory's criteria for determining blood or blood product suitable for reissue? Are they following their policy?

How are untested autologous units, potentially infectious units and reagents stored and segregated to prevent contamination?

If the laboratory does not have an emergency power source for the blood storage equipment and temperature alarm system, how does the laboratory ensure that blood is maintained at the appropriate temperature when a power failure occurs?

If the laboratory is not staffed 24 hours a day, seven days a week, how does it ensure prompt response to an activated alarm (evenings, weekends, and holidays)?

D5557

§493.1271 Standard: Immunohematology.

(d) Retention of samples of transfused blood. According to the laboratory's established procedures, samples of each unit of transfused blood must be retained for further testing in the event of transfusion reactions. The laboratory must promptly dispose of blood not retained for further testing that has passed its expiration date.

Interpretive Guidelines §493.1271(d)

There is no specific timeframe for retaining donor and recipient blood samples. However, it is common practice to keep these samples for a minimum of seven days after each transfusion in case there is a need for retesting.

D5559

§493.1271 Standard: Immunohematology.

(e) Investigation of transfusion reactions.

(e)(1) According to its established procedures, the laboratory that performs compatibility testing, or issues blood or blood products, must promptly investigate all transfusion reactions occurring in facilities for which it has investigational responsibility and make recommendations to the medical staff regarding improvements in transfusion procedures.
(e)(2) The laboratory must document, as applicable, that all necessary remedial actions are taken to prevent recurrences of transfusion reactions and that all policies and procedures are reviewed to assure they are adequate to ensure the safety of individuals being transfused.

Interpretive Guidelines §493.1271(e)(2):

Examine records of transfusion reaction investigations for completeness, accuracy, and promptness. Verify that investigations of transfusion reactions are conducted in accordance with the facility's established protocols. Records must include each step of the investigation, including conclusions and any follow-up.

Probes §493.1271(e)(2):

If problems or technical errors are identified during a transfusion reaction investigation, are corrective actions taken and, as applicable, procedures instituted to prevent a recurrence?

Did the laboratory assess the adequacy of the procedures implemented? Use D5793.

§493.1271 Standard: Immunohematology.

(f) Documentation. The laboratory must document all control procedures performed, as specified in this section.

Interpretive Guidelines §493.1271(f)

All non-transfusion related immunohematology QC records must be retained for at least 2 years. Use D3035

Transfusion-related immunohematology QC records, including but not limited to, donor processing, compatibility testing, and transfusion reaction investigations, must be retained for the timeframe stated at 21CFR 606.160(d).

D5601

§493.1273 Standard: Histopathology.

(a) As specified in §493.1256(e)(3), fluorescent and immunohistochemical stains must be checked for positive and negative reactivity each time of use. For all other differential or special stains, a control slide of known reactivity must be stained with each patient slide or group of patient slides. Reactions(s) of the control slide with each special stain must be documented.

Interpretative Guidelines §493.1273(a)

When condition level deficiencies in Histopathology are in any or all phases of testing, use D5028.

The laboratory must demonstrate that each reagent performs within the specifications established by the laboratory for the test procedure. Documentation of concurrent testing of reagents or acceptable quality control results will satisfy this requirement.

When the laboratory uses a manufacturer's kit, the reagents of the kit must not be combined, mixed, or replaced with components of another kit from a different lot number, unless otherwise permitted and specified by the manufacturer in the package insert. Use D5419.

Laboratories which use automated staining methodologies must follow the manufacturer's instructions. Use D5411.

Flow Cytometry

Staining controls for cell surface immunophenotyping by flow cytometry should consist of either normal, cultured or abnormal cells known to be positive for selected standard antigens and must verify the proper performance of reagents. Frozen or other preserved cells may be used. A negative reagent control must be run for each test cell preparation, and is to consist of monoclonal antibody(ies) of the same species and isotype or equivalent. Negative reagent controls will consist of:

- a) For indirect stains, an irrelevant primary antibody and the same secondary antibody(ies) conjugated with the same fluorochrome(s) used in all relevant test combinations; and*
- b) For direct stains, an irrelevant antibody conjugated to the same fluorochrome and at the same fluorochromes: protein ratio used in all relevant test combinations.*

Probes §493.1273(a)

For flow cell cytometric surface immunophenotyping, is a negative reagent control used to define a threshold for positive staining cells? If not, how does the laboratory define the threshold for positive staining cells?

For each staining run, is a quality control slide tested at the same time patient specimens are tested? Use D5611 for record keeping.

D5603

§493.1273 Standard: Histopathology.

(b) The laboratory must retain stained slides, specimen blocks, and tissue remnants as specified in §493.1105. The remnants of tissue specimens must be maintained in a

manner that ensures proper preservation of the tissue specimens until the portions submitted for microscopic examination have been examined and a diagnosis made by an individual qualified under §§493.1449(b), (l), or (m).

D5605

§493.1273 Standard: Histopathology.

(c) An individual who has successfully completed a training program in neuromuscular pathology approved by HHS may examine and provide reports for neuromuscular pathology.

Interpretative Guidelines §493.1273(c)

HHS approves the American Academy of Neurology Committee for Neuromuscular Pathology Training Program.

D5607

§493.1273 Standard: Histopathology.

(d) Tissue pathology reports must be signed by an individual qualified as specified in paragraph (b) or, as appropriate, paragraph (c) of this section. If a computer report is generated with an electronic signature, it must be authorized by the individual who performed the examination and made the diagnosis.

Interpretative Guidelines §493.1273(d)

The laboratory must ensure that only those individuals qualified to evaluate histopathology specimens can release his or her electronic signature for reporting purposes.

In the event of a computer-generated signature, the laboratory must ensure that the system is protected from use by unauthorized individuals.

D5609

§493.1273 Standard: Histopathology.

(e) The laboratory must use acceptable terminology of a recognized system of disease nomenclature in reporting results.

Interpretative Guidelines §493.1273(e)

“SNOMED®” - Systemized Nomenclature of Medicine is an example of a recognized system of disease nomenclature.

§493.1273 Standard: Histopathology.

(f) The laboratory must document all control procedures performed, as specified in this section.

Interpretative Guidelines §493.1273(f)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were

tested when shipments of reagents, stains, or kits were opened or when the laboratory prepared these materials.

D5613

§493.1274 Standard: Cytology.

(a) Cytology slide examination site. All cytology slide preparations must be evaluated on the premises of a laboratory certified to conduct testing in the subspecialty of cytology.

§493.1274 Standard: Cytology.

(b) Staining. The laboratory must have available and follow written policies and procedures for each of the following, if applicable:

D5615

§493.1274 Standard: Cytology.

(b)(1) All gynecologic slide preparations must be stained using a Papanicolaou or modified Papanicolaou staining method.

Interpretative Guidelines §493.1274(b)(1)

The Papanicolaou staining procedure is a polychrome method that enhances differences in cellular morphology. The procedure utilizes a nuclear stain, hematoxylin and two cytoplasmic counterstains, OG-6 and EA. The Papanicolaou method is used for staining cytologic preparations because it provides well-defined nuclear detail, stains cytoplasm of various cell types different colors, and renders transparent cytoplasm. There are a variety of formulas for making hematoxylin, OG-6, and EA stains. The actual staining technique may vary among laboratories depending on the type of stains used and the laboratories' modification of the staining method. Modifications of the staining procedure must include the four main steps of the standard Papanicolaou staining method: fixation, nuclear staining, cytoplasmic staining, and clearing.

Cytology laboratories may receive reagents, solutions, and stains from a manufacturer in large volume stock containers. For ease in handling, portions of these reagents are usually decanted into smaller working containers, which must be labeled in accordance with §493.1252(c). Some manufacturers do not label stain or reagent containers with the expiration date; however, lot numbers and package inserts refer to this information. (Use D5417 if the laboratory uses materials beyond the expiration dates or the materials have deteriorated.)

If the laboratory uses a manufacturer's kit, the reagents of the kit must not be combined, mixed, or replaced with components of another kit from a different lot number, unless otherwise permitted and specified by the manufacturer in the package insert (use D5419). Laboratories which use automated staining methodologies must follow the manufacturers instructions (use D5411).

The cytology laboratory must document the expiration date of stock reagents, working stains, and solutions made in the laboratory. Use D5415.

Laboratories may use staining procedures, other than the Papanicolaou method, for staining nongynecologic specimens.

Review the written staining procedure for staining gynecologic specimens. Confirm that the written procedures reflect:

- Stains used (i.e., Harris, Gill or other type of hematoxylin, OG-6, modified OG-6, EA36, EA50, EA65, modified EA) or the identity of a combination counterstain;
- Solutions used (water, alcohol, clearing reagent, acid and bluing agent);
- Concentration of each solution used (i.e., percentage (%) of alcohol, acid, ammonium hydroxide or lithium carbonate solution);
- Length of time or number of dips slides are placed in each stain or solution;
- The staining dishes must be labeled to reflect content (not just lids); and
- Procedure for coverslipping slides.

Current time frames must be specified in the procedure manual for each step in the staining of cytology specimens using the Papanicolaou staining method. Adjustments to time frame changes must be documented.

Step-by-step written procedures must be available and followed to prepare nongynecologic specimens.

Use D5403 if any of the above findings is not met.

The laboratory must ensure that the gynecologic and non-gynecologic stains have been tested to ensure predictable staining characteristics on a daily basis. Use D5473.

NOTE: Any fixatives, reagents, or preservatives intended to be used on one liquid-based manufacturer's instrument must not be used on another manufacturer's instrument.

D5617

§493.1274 Standard: Cytology.

(b)(2) Effective measures to prevent cross-contamination between gynecologic and nongynecologic specimens during the staining process must be used.

Interpretative Guidelines §493.1274(b)(2)

The laboratory must develop its own policies and procedures for the prevention of cross-contamination between gynecologic and nongynecologic specimens. The majority of gynecologic specimens are fixed prior to transport to the laboratory. Staining times may differ between gynecologic and nongynecologic specimens. Commonly used methods include separate staining dishes for various specimens (i.e., gynecologic specimens, CSF, sputa, other body fluids), or separate staining times (i.e., gynecologic specimens in the morning and nongynecologic specimens in the afternoon), with the staining dishes washed and stains filtered between staining times.

Probes §493.1274(b)(2)

What does the laboratory do to ensure that cross-contamination between gynecologic and nongynecologic specimens does not occur?

D5619

§493.1274 Standard: Cytology.

(b)(3) Nongynecologic specimens that have a high potential for cross-contamination must be stained separately from other nongynecologic specimens, and the stains must be filtered or changed following staining.

Interpretative Guidelines §493.1274(b)(3)

A monochromatic stain such as toluidine blue may be used to determine the cellularity of nongynecologic specimens. Once a specimen has been concentrated, usually by centrifugation, a small drop of specimen is placed on a slide. A drop of stain is placed next to the specimen, allowed to mix, and coverslipped. Cellularity is evaluated microscopically. Highly cellular specimens have a high potential for cross-contamination. One option would be for the laboratory to stain these specimens after routine staining has been completed.

Laboratories which use automated staining methodologies must follow the manufacturer's instructions. Use D5411.

Probes §493.1274(b)(3)

How is the cellularity of nongynecologic specimens checked prior to cytopreparation (staining)?

What procedure does the laboratory use to determine which specimens must be stained separately?

§493.1274 Standard: Cytology.

(c) Control procedures. The laboratory must establish and follow written policies and procedures for a program designed to detect errors in the performance of cytologic examinations and the reporting of results. The program must include the following:

D5621

§493.1274 Standard: Cytology.

(c)(1) A review of slides from at least 10 percent of the gynecologic cases interpreted by individuals qualified under §§493.1469 or 493.1483, to be negative for epithelial cell abnormalities and other malignant neoplasms (as defined in paragraph (e)(1) of this section).

Interpretive Guidelines §493.1274(c)(1)

The 10 percent rescreen of negative cases is not required for a one-person laboratory consisting of a technical supervisor or a laboratory which only employs pathologists qualified as technical supervisors. However, these laboratories must establish and follow a program to detect errors. This program must include, but is not limited to, cytologic/histologic correlations, retrospective review of negative cases, documentation of initial and rescreening results, and statistics [(c)(2)-(5) of this section].

The laboratory must review all slides from each case selected for rescreen.

(c)(1)(i) The review must be performed by an individual who meets one of the following qualifications:

(c)(1)(i)(A) A technical supervisor qualified under §§493.1449(b) or (k).

(c)(1)(i)(B) A cytology general supervisor qualified under §493.1469.

(c)(1)(i)(C) A cytotechnologist qualified under §493.1483 who has the experience specified in §493.1469(b)(2).

Interpretative Guidelines §493.1274(c)(1)(i)

The laboratory must document which individual(s) are qualified to conduct the 10 percent rescreen. Slides reviewed as part of the 10 percent rescreen must be included in the workload limit of the cytology general supervisor or the cytotechnologist performing the review. Use D5639.

(c)(1)(ii) Cases must be randomly selected from the total caseload and include negatives and those from patients or groups of patients that are identified as having a higher than average probability of developing cervical cancer based on available patient information.

Interpretative Guidelines §493.1274(c)(1)(ii)

The laboratory must have a procedure to determine which slides are rescreened. This procedure should ensure that individuals screening the slides do not know which slides will be chosen for rescreen.

The laboratory must establish criteria to ensure that random negative gynecological cases selected for rescreening include, when possible, cases from patients that are identified as having a higher than average probability for developing cervical cancer.

(c)(1)(iii) The review of those cases selected must be completed before reporting patient results.

D5623

§493.1274 Standard: Cytology.

(c)(2) Laboratory comparison of clinical information, when available, with cytology reports and comparison of all gynecologic cytology reports with a diagnosis of high-grade squamous intraepithelial lesion (HSIL), adenocarcinoma, or other malignant neoplasms with the histopathology report, if available in the laboratory (either on-site or in storage), and determination of the causes of any discrepancies.

Interpretative Guidelines §493.1274(c)(2)

The laboratory must compare clinical information with cytology final reports. For example, an atrophic smear (usually characteristic of a postmenopausal woman) from a 21-year-old female with an LMP (last menstrual period) of 2-weeks-ago constitutes inconsistent findings and must be resolved.

The laboratory must define criteria to determine a discrepancy between a final cytological diagnosis of High Grade Squamous Intraepithelial Lesion (HSIL) or squamous carcinoma, adenocarcinoma or other malignant neoplasias and the correlating histology report.

Cases considered HSIL include: moderate and severe dysplasia, carcinoma in-situ (CIS)/Cervical Intraepithelial Neoplasia (CIN) 2 and CIN 3 or with features suspicious for invasion.

Probes §493.1274(c)(2)

How does the laboratory identify and resolve discrepancies for:

- Clinical information vs. cytology report; and
- Gynecologic cytology report vs. histopathology report?

D5625

§493.1274 Standard: Cytology.

(c)(3) For each patient with a current HSIL, adenocarcinoma, or other malignant neoplasm, laboratory review of all normal or negative gynecologic specimens received within the previous 5 years, if available in the laboratory (either on-site or in storage). If significant discrepancies are found that will affect current patient care, the laboratory must notify the patient's physician and issue an amended report.

Probes §493.1274(c)(3)

How does the laboratory track previous cases on an individual patient?

What criteria does the laboratory use to determine discrepancies when reviewing normal or negative slides from the past five years? How does the laboratory document the review?

How does the laboratory use the retrospective review to assess the analytic system and communicate findings to the appropriate staff? Use D5793

D5627

§493.1274 Standard: Cytology.

(c)(4) Records of initial examinations and all rescreening results must be documented.

D5629

§493.1274 Standard: Cytology.

(c)(5) An annual statistical laboratory evaluation of the number of –

(c)(5)(i) Cytology cases examined;

(c)(5)(ii) Specimens processed by specimen type;

(c)(5)(iii) Patient cases reported by diagnosis (including the number reported as unsatisfactory for diagnostic interpretation);

(c)(5)(iv) Gynecologic cases with a diagnosis of HSIL, adenocarcinoma, or other malignant neoplasm for which histology results were available for comparison;

(c)(5)(v) Gynecologic cases where cytology and histology are discrepant; and

(c)(5)(vi) Gynecologic cases where any rescreen of a normal or negative specimen results in reclassification as low-grade squamous intraepithelial lesion (LSIL), HSIL, adenocarcinoma, or other malignant neoplasms.

Interpretative Guidelines §493.1274(c)(5)(vi)

Low-grade Squamous Intraepithelial Lesions (LSIL) encompasses all lesions that demonstrate cellular changes consistent with human papillomavirus, mild dysplasia, or CIN 1.

D5631

§493.1274 Standard: Cytology.

(c)(6) An evaluation of the case reviews of each individual examining slides against the laboratory's overall statistical values, documentation of any discrepancies, including reasons for the deviation, and, if appropriate, corrective actions taken.

Probes §493.1274(c)(6)

How does the laboratory evaluate each individual's case reviews against the overall laboratory statistics?

What corrective actions are taken to resolve discrepancies? Use D5751.

§493.1274 Standard: Cytology.

(d) Workload limits. The laboratory must establish and follow written policies and procedures that ensure the following:

D5633

§493.1274 Standard: Cytology.

(d)(1) The technical supervisor establishes a maximum workload limit for each individual who performs primary screening.

Interpretative Guidelines §493.1274(d)(1)

The maximum workload limit established by the technical supervisor must be based on each individual's capabilities. A generic workload limit for the laboratory as a whole does not meet this requirement.

Probes §493.1274(d)(1)

What criteria does the technical supervisor use to determine the slide limit for each person who examines slides?

D5635

§493.1274 Standard: Cytology.

(d)(1)(i) The workload limit is based on the individual's performance using evaluations of the following:

Interpretative Guidelines §493.1274(d)(1)(i)

The technical supervisor maintains documentation of the slide performance and provides feedback.

Probes §493.1274(d)(1)(i)

What records are maintained to document the technical supervisor's evaluation of the slide performance of each individual?

(d)(1)(i)(A) Review of 10 percent of the cases interpreted as negative for the conditions defined in paragraph (e)(1) of this section.

(d)(1)(i)(B) Comparison of the individual's interpretation with the technical supervisor's confirmation of patient smears specified in paragraphs (e)(1) and (e)(3) of this section.

Probes §493.1274(d)(1)(i)(B)

How does the technical supervisor ensure that feedback is provided on slide examination performance to each person evaluating slides?

What mechanism is used to allow individuals an opportunity to discuss instances of misdiagnosis?

D5637

§493.1274 Standard: Cytology.

(d)(1)(ii) Each individual's workload limit is reassessed at least every 6 months and adjusted when necessary.

Probes §493.1274(d)(1)(ii)

What criteria does the technical supervisor use to determine when a workload adjustment is needed?

How are records maintained to document that workload records are reassessed at least every six months and adjusted when necessary?

D5639

§493.1274 Standard: Cytology.

(d)(2) The maximum number of slides examined by an individual in each 24-hour period does not exceed 100 slides (one patient specimen per slide; gynecologic, nongynecologic, or both) irrespective of the site or laboratory. This limit represents an absolute maximum number of slides and must not be employed as an individual's performance target. In addition—

Interpretative Guidelines §493.1274(d)(2)

The maximum total number of slides an individual may screen is 100 per 24 hours regardless of site or laboratory. Although the regulation establishes this maximum number, not every individual will be able to accurately examine 100 slides in 24 hours. The laboratory must establish how many slides can be screened per day for each individual. Refer to §493.1274(d)(1) to insure that the technical supervisor has established a maximum number of slides that each individual is capable of evaluating. The laboratory must ensure that persons employed at other sites or locations do not exceed the maximum of 100 slides in 24 hours .

This 100-slide limit is also applicable to those technical supervisors who examine previously unevaluated cytology specimens.

Probes §493.1274(d)(2)

How does the laboratory ensure that each individual examining slides (cytotechnologists, cytology general supervisors and technical supervisors in cytology, as applicable) examines no more than 100 slides in a 24-hour period regardless of site or location?

(d)(2)(i) The maximum number of 100 slides is examined in no less than an 8-hour workday;

Probes §493.1274(d)(2)(i)

What records are used to verify that the maximum number of 100 slides is examined in no less than 8 hours, especially in the situation in which individuals screen slides at different sites or locations?

D5641

§493.1274 Standard: Cytology.

(d)(2)(ii) For the purposes of establishing workload limits for individuals examining slides in less than an 8-hour workday (includes full-time employees with duties other than slide examination and part-time employees), a period of 8 hours is used to prorate the number of slides that may be examined.

The formula--

$$\frac{\text{Number of hours examining slides} \times 100}{8}$$

is used to determine maximum slide volume to be examined;

D5643

§493.1274 Standard: Cytology.

(d)(2)(iii) Nongynecologic slide preparations made using liquid-based slide preparatory techniques that result in cell dispersion over one-half or less of the total available slide may be counted as one-half slide; and

Interpretative Guidelines §493.1274(d)(2)(iii)

Nongynecologic slide preparations made using automated, semi-automated or other liquid-based slide preparatory techniques include specimens prepared by centrifugation, cytocentrifugation, filtering techniques or monolayering techniques. Any instrument used to assist in the adherence of cells to the slide is considered to meet this requirement. This requirement refers to slide preparatory techniques, not liquid based coverslips. Slides prepared by traditional methods (usually smears prepared by hand) are not included.

<u>Maximum Workload Limits for Nongynecologic Specimens</u>	
<i>Traditional Smear Technique</i>	<i>100 Slides</i>
<i>Automated, Semi-Automated, Liquid-Based</i>	<i>200 Slides</i>
<i>Combination of Techniques</i>	<i>100 - 200 Slides</i>
<i>(Based on Prorated Time)</i>	

(d)(2)(iv) Technical supervisors who perform primary screening are not required to include tissue pathology slides and previously examined cytology slides (gynecologic and nongynecologic) in the 100 slide workload limit.

D5645

§493.1274 Standard: Cytology.

(d)(3) The laboratory must maintain records of the total number of slides examined by each individual during each 24-hour period and the number of hours spent examining slides in the 24-hour period irrespective of the site or laboratory.

Interpretative Guidelines §493.1274(d)(3)

Verify that the laboratory monitors the number of slides examined by each individual and the number of hours spent examining slides.

D5647

§493.1274 Standard: Cytology.

(d)(4) Records are available to document the workload limit for each individual.

Probes §493.1274(d)(4)

What records are maintained of each individual's workload limit when various types of slides are evaluated?

§493.1274 Standard: Cytology.

(e) Slide examination and reporting. The laboratory must establish and follow written policies and procedures that ensure the following:

D5649

§493.1274 Standard: Cytology.

(e)(1) A technical supervisor confirms each gynecologic slide preparation interpreted to exhibit reactive or reparative changes or any of the following epithelial cell abnormalities:

(e)(1)(i) Squamous Cell

Interpretative Guidelines §493.1274(e)(1)(i)

Note: This requirement is in addition to the review and confirmation by a technical supervisor of all nongynecologic preparations as described under §493.1274(e)(3).

Probes §493.1274(e)(1)(i)

How does the laboratory ensure that the technical supervisor confirms every slide containing cells exhibiting reactive, reparative, atypical squamous/glandular cells, LSIL, HSIL, and all carcinomas?

(e)(1)(i)(A) Atypical squamous cells of undetermined significance (ASC-US) or cannot exclude HSIL (ASC-H).

(e)(1)(i)(B) LSIL-Human papillomavirus (HPV)/mild dysplasia/cervical intraepithelial neoplasia 1 (CIN 1).

(e)(1)(i)(C) HSIL-moderate and severe dysplasia, carcinoma in situ (CIS)/CIN 2 and CIN 3 or with features suspicious for invasion.

(e)(1)(i)(D) Squamous cell carcinoma.

(e)(1)(ii) Glandular Cell

(e)(1)(ii)(A) Atypical cells not otherwise specified (NOS) or specified in comments (endocervical, endometrial, or glandular).

(e)(1)(ii)(B) Atypical cells favor neoplastic (endocervical or glandular).

(e)(1)(ii)(C) Endocervical adenocarcinoma in situ.

(e)(1)(ii)(D) Adenocarcinoma endocervical, adenocarcinoma endometrial, adenocarcinoma extrauterine, and adenocarcinoma NOS.
(e)(1)(iii) Other malignant neoplasms.

D5651

§493.1274 Standard: Cytology.

(e)(2) The report of gynecologic slide preparations with conditions specified in paragraph (e)(1) of this section must be signed to reflect the technical supervisory review or, if a computer report is generated with signature, it must reflect an electronic signature authorized by the technical supervisor who performed the review.

Interpretative Guidelines §493.1274(e)(2)

The laboratory must ensure that the technical supervisor is the only individual to release his or her electronic signature for reports requiring technical supervisory review.

If an electronic signature is used, the laboratory must ensure that the system is protected from use by unauthorized individuals.

D5653

§493.1274 Standard: Cytology.

(e)(3) All nongynecologic preparations are reviewed by a technical supervisor. The report must be signed to reflect technical supervisory review or, if a computer report is generated with signature, it must reflect an electronic signature authorized by the technical supervisor who performed the review.

Interpretative Guidelines §493.1274(e)(3)

The laboratory must ensure that the technical supervisor:

- *Is the only individual to release his or her electronic signature for reports requiring technical supervisory review; and*
- *Reviews all nongynecologic cytological preparations.*

If an electronic signature is used, the laboratory must ensure that the system is protected from use by unauthorized individuals.

D5655

§493.1274 Standard: Cytology.

(e)(4) Unsatisfactory specimens or slide preparations are identified and reported as unsatisfactory.

Interpretative Guidelines §493.1274(e)(4)

The report should clearly specify when the slide is unsatisfactory for evaluation. Unsatisfactory slide preparations should not be reported as negative or normal. Use D5805.

Probes §493.1274(e)(4)

What criteria have been developed for categorizing a slide preparation as unsatisfactory (e.g., scant cellularity, obscuring blood, obscuring inflammation, or lack of endocervical component)?

D5657

§493.1274 Standard: Cytology.

(e)(5) The report contains narrative descriptive nomenclature for all results.

Interpretative Guidelines §493.1274(e)(5)

In cytology, great variation exists among the systems and terms a laboratory may use to report patient results on cytology reports. The laboratory must specify the descriptive nomenclature used for reporting patient results. This nomenclature must define the criteria used to classify patient results in a particular category in a clear and concise manner to ensure that all employees report patient results in a uniform, consistent manner. Use of the Papanicolaou numerical system without narrative description is not acceptable.

The Bethesda System is an example of a recognized system of narrative descriptive nomenclature for gynecologic cytology.

Probes §493.1274(e)(5)

When cytology evaluations are recorded on worksheets in "code" how does the laboratory ensure that the correct interpretation is used in reporting the results? Use D5801.

D5659

§493.1274 Standard: Cytology.

(e)(6) Corrected reports issued by the laboratory indicate the basis for correction.

Probes §493.1274(e)(6)

How does the laboratory indicate that the report is a corrected report (to avoid confusion with the initial report)? Use D5821.

How does the laboratory include the cause or reason for the correction in the report?

§493.1274 Standard: Cytology.

(f) Record and slide retention.

(f)(1) The laboratory must retain all records and slide preparations as specified in §493.1105.

D5661

§493.1274 Standard: Cytology.

(f)(2) Slides may be loaned to proficiency testing programs in lieu of maintaining them for the required time period, provided the laboratory receives written acknowledgment of the receipt of slides by the proficiency testing program and maintains the acknowledgment to document the loan of these slides.

(f)(3) Documentation of slides loaned or referred for purposes other than proficiency testing must be maintained.

D5663

§493.1274 Standard: Cytology.

(f)(4) All slides must be retrievable upon request.

Probes §493.1274(f)(4)

If the laboratory loans slides, what protocol has been established to ensure prompt return of slides, when necessary?

D5665

§493.1274 Standard: Cytology.

(g) Automated and semi-automated screening devices. When performing evaluations using automated and semi-automated screening devices, the laboratory must follow manufacturer's instructions for preanalytic, analytic, and postanalytic phases of testing, as applicable, and meet the applicable requirements of this subpart K.

Interpretative Guidelines §493.1274(g)

Some automated devices, such as instruments where only a portion of the slide is reviewed, may have a higher workload limit than 100 slides. This must be stated in the manufacturer's product insert to be applicable. However, the maximum workload limit for those slides which require 100% manual review (as a result of automated or semi-automated analysis OR in the routine workload) remains 100 slides.

Probes §493.1274(g)

When technology (automated/semi-automated devices) is introduced into the laboratory, how does the laboratory ensure its operation is within the specifications of previous methods used by the laboratory?

Some automated devices remove a percentage of the slides from the workload. How does the laboratory ensure that the correct slides are archived?

§493.1274 Standard: Cytology.

(h) Documentation. The laboratory must document all control procedures performed, as specified in this section.

Interpretative Guidelines §493.1274(h)

QC records should include lot numbers, date prepared/opened, expiration dates, the actual measurements, reactions, and/or observations and demonstrate that controls were tested when shipments of reagents, stains, or kits were opened or when the laboratory prepared these materials.

The actual measurements(s) taken, reactions and/or observations must be recorded. However, do not dictate the acceptable format for documentation.

The laboratory must maintain documentation to demonstrate that ten percent of the negative cases were rescreened.

All QC records must be maintained for two years, for example: five year retrospective review, 10 percent rescreens, cytology/histology correlations, cytotechnologist's

performance evaluations, individual's and laboratory's statistics (use D3031). Use D3043 for retention of glass slides and D3041 for retention of patient test reports.

The laboratory must document the evaluation of quality control data and ensure that corrective actions are effective. Use D5793.

Probes §493.1274(h)

What information is documented on the quality control records?

What records does the laboratory maintain to document that stains are filtered or changed when necessary?

D5681

§493.1276 Standard: Clinical cytogenetics.

(a) The laboratory must have policies and procedures for ensuring accurate and reliable patient specimen identification during the process of accessioning, cell preparation, photographing or other image reproduction technique, photographic printing, and reporting and storage of results, karyotypes, and photographs.

Interpretive Guidelines §493.1276(a)

When condition level deficiencies in Clinical Cytogenetics are in any or all phases of testing, use D5034.

Determine which of the following services may be provided:

- Tissue Cultures (e.g., skin, lung, product of conception);
- Bone Marrow Cultures;
- Solid Tumors;
- Lymph Nodes;
- Chorionic Villus Samples (CVS);
- Peripheral Lymphocyte Cultures;
- Amniotic Fluid Cultures;
- High resolution chromosome analysis;
- Special techniques (e.g., Fragile "X" Studies, Chromosome Breakage analysis);
- Karyotype analysis (photographic and/or computer methods);
- Transplant studies;
- Chromosome staining (banding techniques) such as:
 - Quinacrine fluorescence (Q Banding);
 - Giesma/trypsin (G Banding);
 - Sodium phosphate/acridine or giesma/heat (R Banding);
 - Barium hydroxide/heat (C Banding);
 - Nuclear Organizing Region - Silver Stain (NOR);
 - Distamycin A/4-6-diamidino-2-phenylindole (DA/DAPI); or
 - Giemsa 11 (pH 11.0 for heterochromatin) (G 11).

NOTE: The above listing is not intended to be all-inclusive.

Review a sample of patient case files to determine if it is possible to go from the accession number to the patient's file with karyotypes, report and observation records, the microscope slide, photographs or requisition forms.

Probes §493.1276(a)

When photographs are taken, are the coordinates of the microscope noted for each cell selected? If not, how does the laboratory identify the cell for future reference?

What system does the laboratory use to ensure that records reflect accurate patient identification when:

- Photographing chromosome spreads;
- Using computer systems to assist in karyotyping; or
- Storing photographic images of chromosomes and chromosomes spreads?

D5683

§493.1276 Standard: Clinical cytogenetics.

(b) The laboratory must have records that document the following:

(b)(1) The media used, reactions observed, number of cells counted, number of cells karyotyped, number of chromosomes counted for each metaphase spread, and the quality of the banding

(b)(2) The resolution is appropriate for the type of tissue or specimen and the type of study required based on the clinical information provided to the laboratory.

(b)(3) An adequate number of karyotypes are prepared for each patient.

Interpretive Guidelines §493.1276(b)(1)-(b)(3)

<u>Culture Type</u>	Minimum Number of Spreads Counted per Patient	Minimum Number of Cells Analyzed per Patient
Amniotic Fluid		
Flasks	15 cells from at least 2 independent primary cultures	5 cells from at least 2 independent primary cultures
<u>in situ</u>	15 cells from at least 10 colonies from 2 independent primary cultures	5 cells from different colonies and split between different primary cultures

Many laboratories use a combination of the flask and in situ culture methods or use the flask method as a backup for the in situ method.

Chorionic Villus		
Direct	15 cells	5 cells
Culture	as in amniotic fluid, flask technique	
Peripheral Blood		
Constitutional	20 cells	5 cells
Possible sex chromosome abnormality	30 cells (total count)	5 cells
<u>Culture Type</u>	Minimum Number of Spreads Counted per Patient	Minimum Number of Cells Analyzed per Patient
Blood (cancer)	20 cells	20 cells

Bone Marrow (cancer)	20 cells	20 cells
Tissue Fibroblasts	15 cells from 2 independent cultures	5 cells split between 2 independent cell cultures

For confirmation of chromosomally abnormal amniotic fluid results, or familial chromosome abnormality, examination of fewer cells is permitted.

A number of factors may influence the quality of the metaphase spreading (e.g., humidity, air flow, cell concentration, and cell storage conditions).

An analysis of at least 50 cells is recommended when:

- *Single trisomic cells are found during a study;*
- *Mosaicism is suspected on the basis of a phenotype not correlating with the karyotype during the study; or*
- *Sex chromosome abnormalities are suspected.*

Additionally, when mosaicism is suspected, ensure that adequate number of cells or nuclei are scored.

- *Follow manufacturer's instructions for the use of the probe in accordance with the FDA requirements for "Analyte Specific Reagents (ASR)."*
- *Establish or verify test system performance using each new probe and each new lot of probe in accordance with D5421 or D5423; thereafter the laboratory must ensure test methodology performance in accordance with D5411.*
- *Establish criteria for scoring the number of probe signals and the number of cells to be examined. Use D5425.*

For fragile X analysis:

- *Males - at least 50-100 cells should be scored for negative analysis.*
- *Females - at least 100-150 cells should be scored for negative analysis.*

The presence of the Xq27.3 fragile site should be confirmed with chromosome banding.

Fragile X studies require low folate medium and media which includes treatment with an antimetabolite such as fluorodeoxyuridine (FUdR), methotrexate, excess thymidine, fluorodeoxycytidine (FdC) or other proven induction systems.

General guidance:

Examine the karyotypes and a slide from among the laboratory cases and determine if the quality of banding and resolution was sufficient to render the reported interpretation. Examination of the long arm on the 18th chromosome should demonstrate at least two distinct dark staining G-bands at the 400 band level.

Verify that the laboratory's policy establishes a specific band level of resolution that would be dependent upon the study requested.

High resolution chromosome analysis should refer to studies done above the 550 band stage. (Above 650 band stage for an unfocused study. A focused study should be done at a level of resolution at which the band in question is clearly separated from surrounding bands in one member of the homologous pair in question.) Use D5683.

Probes §493.1276(b)(1)-(b)(3)

For fragile X analysis, if a folate deficient medium is not used as described above, how does the laboratory assure the validity of the test system and the accuracy of results? Use D5411 or D5413, as applicable.

How many photographic and/or computerized karyotypes are prepared from each cell line? (A minimum of 2 is recommended.)

What band level of resolution is used by the laboratory to rule out structural defects (i.e., routine or 400-500 band stage, or high resolution or 650-850 band stage)?

D5685

§493.1276 Standard: Clinical cytogenetics.

(c) Determination of sex must be performed by full chromosome analysis.

D5687

§493.1276 Standard: Clinical cytogenetics.

(d) The laboratory report must include a summary and interpretation of the observations, number of cells counted and analyzed, and use the International System for Human Cytogenetic Nomenclature.

Probes §493.1276(d)

Does the laboratory report include:

- *Type of banding method used, if applicable;*
- *Stage of cell mitosis when banded;*
- *Number of cells counted and analyzed microscopically;*
- *Number of cells from which photographic or computerized karyotypes were prepared; and*
- *Estimate of the banding resolution achieved?*

Does the laboratory, where appropriate, ensure that FISH clinical interpretations are made in conjunction with standard cytogenetic analyses and evaluated against patient medical history and other diagnostic test results?

Preliminary reports of karyotypes based on less than full analysis are acceptable if the diagnosis is clear.

For what types of cultures are preliminary reports issued? These may include, but are not limited to, the following:

- *Bone marrow analysis (within 14 days);*
- *Unstimulated blood cultures (within 14 days); and*
- *Lymphocytes from newborns (within 7 days).*

What is the average length of time for reporting (use D5801 or D5815, as appropriate):

- *Amniotic fluid cell cultures (90% of prenatal diagnosis cases should be signed out in 21 days);*
- *Routine lymphocyte cultures (approximately 4-5 weeks); and*
- *Fibroblast cultures (approximately 2-3 months)?*

Do records document:

- Observations made concurrently with the performance of each step in the examination of specimens/cultures (use D5683); and
- The number of cases reviewed, signed out and/or the frequency of failed or sub-optimal cultures?

§493.1276 Standard: Clinical cytogenetics.

(e) The laboratory must document all control procedures performed, as specified in this section.

Probes §493.1276(e)

Each day of use, does the laboratory test the positive and negative reactivity of staining materials to ensure predictable staining characteristics? Use D5473.

Does the laboratory, concurrent with the initial use, check each batch of media for pH (amniotic cell cultures should be kept between pH 6.8 and 7.8), sterility, and ability to support growth? Use D5477.

Does the laboratory employ an alternative procedure for the immediate assessment and monitoring of all testing over time? For example: Control materials are not routinely available to demonstrate chromosome abnormalities for linkage, breakage or translocation, but the laboratory must demonstrate an alternative mechanism for detecting chromosome abnormalities to be analyzed. Use 5485.

An alternative procedure might include spit sample with another laboratory, repeat patient specimen, special stains, FISH assays, and/or molecular assays.

§493.1278 Standard: Histocompatibility.

(a) General. The laboratory must meet the following requirements.

Probes: §493.1278(a):

When condition level deficiencies in Histocompatibility are in any or all phases of testing, cite D5038.

D5729

§493.1278 Standard: Histocompatibility.

(a)(1) An audible alarm system must be used to monitor the storage temperature of specimens (donor and recipient) and reagents. The laboratory must have an emergency plan for alternate storage.

Interpretative Guidelines §493.1278(a)(1)-(a)(2):

Ultra low (-80°C) freezers and liquid nitrogen (LN2) reservoirs are common in these laboratories. LN2 reservoirs should be monitored to ensure adequate supply of LN2 at all times.

Verify that the laboratory has an audible alarm system for freezers and refrigerators where critical patient specimens and test reagents are stored. The laboratory should

have established the temperature at which the audible alarm will activate. Determine if the laboratory has an emergency power source for this alarm system in the event of an electrical failure. If emergency power is not available, the laboratory should have policies/procedures on how to ensure a prompt response to an activated alarm, 24 hours a day, 7 days a week, including holidays.

An emergency plan for alternate storage of historic patient serum specimens necessary for pre-transplant crossmatching is critical. Verify that the laboratory has an emergency plan for alternate storage appropriate for its operational needs.

D5731

§493.1278 Standard: Histocompatibility.

(a)(2) All patient specimens must be easily retrievable.

Interpretative Guidelines §493.1278(2):

Patient specimens needed for pre-transplant testing should be stored on-site.

D5733

§493.1278 Standard: Histocompatibility.

(a)(3) Reagent typing sera inventory prepared in-house must indicate source, bleeding date and identification number, reagent specificity, and volume remaining.

D5735

§493.1278 Standard: Histocompatibility.

(a)(4) If the laboratory uses immunologic reagents (for example, antibodies, antibody-coated particles, or complement) to facilitate or enhance the isolation of lymphocytes, or lymphocyte subsets, the efficacy of the methods must be monitored with appropriate quality control procedures.

Interpretative Guidelines 493.1278(a)(4):

Lymphocytes can be isolated from peripheral blood, lymph nodes and spleen. These cells can be further separated into subsets such as T cells and B cells. Examples of commonly used commercial immunologic reagents include immunomagnetic beads and monoclonal reagents. The laboratory should determine the quality (cell viability), the quantity (final yield), subset specificity (T cell, B cell, etc.), and purity (contaminating cells removed) of the final cell preparation. The laboratory should have policies and/or procedures for assessment of the efficacy of these reagents to include criteria for acceptability. For deficiencies related to the procedure, use D5403; for control material acceptability, use D5469.

The subset specificity of each lot of immunomagnetic beads should be verified with antiserum specific for each cell type (e.g., T cell beads with anti-T-lymphocyte serum).

D5737

§493.1278 Standard: Histocompatibility.

(a)(5) Participate in at least one national or regional cell exchange program, if available, or develop an exchange system with another laboratory in order to validate interlaboratory

reproducibility.

Interpretative Guidelines §493.1278(a)(5):

Programs offered by proficiency testing companies and cell exchanges for histocompatibility laboratories are readily available. An example of a regional exchange program is the Southeastern Organ Procurement Foundation (SEOPF). UCLA provides an international monthly exchange program with sera, cells and DNA. The College of American Pathologists (CAP) and the American Society for Histocompatibility and Immunogenetics (ASHI) each offer programs that assess the primary areas of testing in histocompatibility laboratories by test techniques (i.e., antibody screening and identification, HLA typing for Class I (HLA-A, B, C) and Class II (HLA-DR, DQ), lymphocyte crossmatching (T cell and B cell)).

Laboratories participating in a local exchange should record information concerning the frequency of exchange and the grading system.

Cite a deficiency if the laboratory is not enrolled in a cell exchange program or is enrolled in a program, but fails to return the results. A laboratory's performance in a regional or national exchange program should be evaluated against a peer group performing the same technique.

D5739

§493.1278 Standard: Histocompatibility.

(b) HLA typing. The laboratory must do the following:

Interpretative Guidelines §493.1278(b):

HLA (Human Leukocyte Antigens) typing is the identification of histocompatibility antigens and/or alleles. HLA typing is performed by serologic or molecular methods.

Serologic typing is usually performed by incubating viable lymphocytes with antisera of known HLA specificities. Antibodies will bind cells with the corresponding HLA antigen(s) on their surface. When complement is added to an immune complex, it binds to the complex causing cell death. The surface of the lymphocyte becomes permeable to stains and this positivity is determined microscopically.

HLA typing using nucleic acid (DNA) and primers and/or probes involves using the polymerase chain reaction (PCR) to amplify HLA sequences of interest which are detected by gel electrophoresis, ELISA or by fluorescence detection using flow cytometry.

(b)(1) Use a technique(s) that is established to optimally define, as applicable, HLA Class I and II specificities.

Interpretative Guidelines §493.1278(b)(1):

HLA CLASS I specificities include HLA-A, B, Cw.

HLA CLASS II specificities include HLA-DR, DQ, and DP.

Verify that the laboratory has validated the reagents and methods it uses. For deficiencies related to verification of methods, use D5421; for establishment of methods, use D5423.

(b)(2) HLA type all potential transplant recipients at a level appropriate to support clinical

transplant protocol and donor selection.

Interpretative Guidelines §493.1278(b)(2):

The laboratory should be an active participant of the transplant center's clinical program. It should provide the technical assistance and pertinent data necessary to help establish transplant protocols for solid organ, tissue and cellular transplants and transfusions. Each protocol should specify what HLA specificities should be identified and at what level this testing needs to be performed. HLA Class I and Class II typing must be performed in accordance with the protocol.

(b)(3) HLA type cells from organ donors referred to the laboratory.

(b)(4) Use HLA antigen terminology that conforms to the latest report of the World Health Organization (W.H.O.) Committee on Nomenclature. Potential new antigens not yet approved by this committee must have a designation that cannot be confused with W.H.O. terminology.

(b)(5) Have available and follow written criteria for the following:

D5741

§493.1278 Standard: Histocompatibility.

(b)(5)(i) The preparation of cells or cellular extracts (for example, solubilized antigens and nucleic acids), as applicable to the HLA typing technique(s) performed.

Interpretative Guidelines §493.1278(b)(5)(i):

The laboratory's procedure manual should contain cell and /or DNA isolation procedures for each type of specimen it uses (e.g., peripheral blood, lymph nodes and spleen, cell cultures, filter paper blood spots, buccal swabs).

Laboratories should assess pretest viability of cells prior to dotting on typing trays. They may use trypan blue stain, wet preps, etc. Verify that the laboratory maintains records of this activity. For most techniques, viability should exceed 80%.

Determine if the laboratory has verified their extraction method. Use D5421.

D5743

§493.1278 Standard: Histocompatibility.

(b)(5)(ii) Selecting typing reagents, whether prepared in-house or commercially.

Interpretative Guidelines §493.1278(b)(5)(ii)

For HLA complement dependent lymphocytotoxicity typing, each batch of complement must be tested to determine that it mediates cytotoxicity (cell death) in the presence of a specific HLA antibody, but is not cytotoxic in the absence of a specific antibody. The test should ensure that it is maximally active at least one dilution beyond that intended for use. The test should be carried out with at least two antibodies known to react with at least two different cells (positive control), and at least one cell which should not react (negative control). A strong and a weak antibody should be selected for the test. Serial dilutions of a single serum may also be used. Verify that the laboratory has performed complement quality control and that an optimum dilution has been selected and documented. Complement is temperature sensitive (labile) and should be retitered periodically to ensure its activity. Determine if the laboratory has complement retitering policies/procedures.

The results of each batch/lot of reagents (typing trays) whether commercially made or prepared in-house must be reviewed to determine which sera failed to react as expected (false negative reactions) and which sera had unexpected reactions (false positive reactions). Future tray preparation and interpretation of commercially purchased trays should be evaluated and revised based on the results of these reviews.

Probes §493.1278(b)(5)(ii):

What criteria were used to determine the acceptability of each batch of complement for HLA serologic assays?

How does the laboratory select the typing trays it uses for each patient?

D5745

§493.1278 Standard: Histocompatibility.

(b)(5)(iii) Ensuring that reagents used for typing are adequate to define all HLA-A, B and DR specificities that are officially recognized by the most recent W.H.O. Committee on Nomenclature and for which reagents are readily available.

Interpretative Guidelines §493.1278(b)(5)(iii):

Antisera for less frequent and rare specificities may be unavailable to laboratories. It is good laboratory practice for each HLA antigen to be defined by at least two operationally monospecific sera. Typing for (HLA) class I or class II antigens must employ a sufficient number of antisera or monoclonal antibodies to clearly define all the antigens for which the laboratory tests. For example: If multispecific sera must be used, at least three partially non-overlapping sera should be used to define each HLA-antigen. For each HLA-DR and HLA-DQ antigen to be defined, at least 3 operationally monospecific sera should be used. If multispecific sera must be used, at least 5 partially non-overlapping sera should be used.

The laboratory should demonstrate that typing sera reactions are recorded, reviewed and used to modify locally prepared typing trays and interpret commercial tray specificities.

Primer and/or probe sequence, specificity and sensitivity should be defined with reference material (previously typed DNA). For typing methods using probe technology, verify whether optimum hybridization temperatures have been verified or established for each probe.

The laboratory should demonstrate that reference material testing is recorded regularly, reviewed and used to modify locally prepared reagents, as well as interpret commercial primer and/or probe specificities.

Probes §493.1278(b)(5)(iii):

How are the specificities of new typing sera, primers and probes (whether local or commercial) verified, e.g., by parallel testing with known cells or DNA?

How does the laboratory report HLA typings performed by serology and DNA (i.e., follow the W.H.O. nomenclature list)? Are antigens and alleles reported appropriately?

D5747

§493.1278 Standard: Histocompatibility.

(b)(5)(iv) The assignment of HLA antigens.

Interpretative Guidelines §493.1278(b)(5)(iv):

Criteria for antigen and/or allele assignment must take into account basic principles of genetic inheritance.

Examples:

1. No more than 2 antigens or alleles per HLA-A, B, and DR locus can be assigned to any patient; e.g., antigens HLA-A2, A24; B46, B61; DR8, 14; alleles HLA-A*02XX, 24XX; B*4002, 4601; DRB1*0803, 1401. Public specificities may be observed; i.e. for HLA-B, additional specificities of Bw4 and/or Bw6 are reported, for Class II antigens, additional gene products of DR51, DR52 and/or DR53 are reported.
2. When family studies are performed, typing interpretations should be in accordance with genetic relationships (i.e., haplotype assignments, determination of homozygosity at a particular locus).

Verify that the laboratory has established acceptability criteria for assignment of HLA antigens and/or alleles. Examples for alleles include signal intensity, band clarity and migration, specificity, and procedures to resolve ambiguous alternative combinations.

Determine if testing personnel follow the scoring and reporting system defined in the procedure manual. Two independent interpretations are recommended for each DNA analysis. Determine if the laboratory has validated computer software for the analysis of antigens and/or alleles.

D5749

§493.1278 Standard: Histocompatibility.

(b)(5)(v) When antigen redefinition and retyping are required.

Interpretative Guidelines §493.1278(b)(5)(v):

Verify that the laboratory has policies and procedures for antigen and/or allele redefinition and retyping. Records should indicate that results from redefinition and retyping are evaluated and that patient typings are updated accordingly. Discrepancies identified as the result of this activity should be documented and resolved. Use D5775.

D5751

§493.1278 Standard: Histocompatibility.

(b)(6) Check each HLA typing by testing, at a minimum the following:

(b)(6)(i) A positive control material.

(b)(6)(ii) A negative control material in which, if applicable to the technique performed, cell viability at the end of incubation is sufficient to permit accurate interpretation of results. In assays in which cell viability is not required, the negative control result must be sufficiently different from the positive control result to permit accurate interpretation of results.

(b)(6)(iii) Positive control materials for specific cell types when applicable (that is, T cells, B cells, and monocytes).

Interpretative Guidelines §493.1278(b)(6):

Each HLA-A, B, C or supplemental Class I typing tray must include at least one positive control serum, previously shown to react with all lymphocytes, and one negative control serum which has been demonstrated to be non-cytotoxic. HLA-DR and DQ typing trays must include a positive control serum, previously shown to react with only B cells, and

one negative control serum which has been demonstrated to be non-cytotoxic.

Cell controls must be tested with each batch/lot/shipment of typing trays. Typing results are invalid if controls fail to react as expected. The negative control should either be one previously shown to lack antibody or should be from a healthy male with no history of blood transfusion. Cell viability in the negative control well at the end of the incubation must be sufficient to permit accurate interpretation of results. For most techniques, viability should exceed 80%. However, when less than optimal specimens, such as cadaver and mailed specimens, this threshold may not be met.

For DNA typing, negative control wells or wells with no DNA should not give a positive result (the presence of a band), however, internal controls should give a positive result. DNA reference material must be tested with each lot of typing reagents. Primers and/or probes must be tested for allele specificity with reference material.

D5753

§493.1278 Standard: Histocompatibility.

(c) Disease-associated studies. The laboratory must check each typing for disease-associated HLA antigens using control materials to monitor the test components and each phase of the test system to ensure acceptable performance.

Interpretative Guidelines §493.1278(c):

Disease association studies are single or limited antigen typings usually performed by serologic typing methods and more rarely performed by flow cytometric methods.

Positive and negative controls must be run with each test.

Control cells must be tested with each lot and shipment of reagents. Use D5469.

For serologic typings, the control cells should include at least two cells known to express the specified antigen and two cells known to express cross-reacting antigens that might be confused with the specific antigen. Control cells should also include at least two cells lacking the specific and cross-reacting antigen.

For typing sera acceptability, use D5745.

D5755

§493.1278 Standard: Histocompatibility.

(d) Antibody Screening. The laboratory must do the following:

(d)(1) Use a technique(s) that detects HLA-specific antibody with a specificity equivalent or superior to that of the basic complement-dependent microlymphocytotoxicity assay.

(d)(2) Use a method that distinguishes antibodies to HLA Class II antigens from antibodies to Class I antigens to detect antibodies to HLA Class II antigens.

(d)(3) Use a panel that contains all the major HLA specificities and common splits. If the laboratory does not use commercial panels, it must maintain a list of individuals for fresh panel bleeding.

Interpretative Guidelines §493.1278(d)(1)-(d)(3):

An antibody screen is performed to identify whether a patient's serum contains antibodies to one or more HLA antigens. This is accomplished by screening the serum against target antigens from a suitable panel appropriate for the population served, i.e., a variety

of ethnic groups. Results are expressed as percent reactive antibodies (PRA).

The panel of antigens used must include all of the HLA antigens to which the most common HLA antibodies are formed. Cell panels of known HLA type must be available to prove the specificity of new antibodies. The serum cell panel should be consistent from month to month and from lot to lot. Verify that the frequency of each antigen represented does not vary significantly.

An example of PRA differences from panel to panel:

If a patient demonstrates a HLA-A2 antibody and the cell panel contains 15 A2 positive cells out of 100, the patient's PRA on this tray will be 15%. If the same patient is tested against a panel where there are 37 A2 positive cells out of 100, the patient's PRA will increase to 37%. The number of A2 positive cells on this laboratory's cell panel should reflect the frequency observed in the population it serves; e.g., 15-20% of the local population possess the HLA-A2 antigen.

If the laboratory tests for antibodies to Class II antigens, the laboratory should have a procedure for removing Class I antibodies or should use purified Class II antigens. Class II antigens (HLA-DR, DQ) are found only on the B cell subset of lymphocytes. B cells also have a high density of Class I antigens (HLA-A, B, C), which are found on all nucleated cells. If a patient has a significant titer of Class I antibodies, it may result in a false positive Class II antibody test result. Platelet absorption is one method of removing the Class I antibodies.

Verify that the laboratory's antibody screening technique is as sensitive as the crossmatch method it uses to ensure optimum compatibility.

D5757

§493.1278 Standard: Histocompatibility.

(d)(4) Make a reasonable attempt to have available monthly serum specimens for all potential transplant recipients for periodic antibody screening and crossmatch.

(d)(5) Have available and follow a written policy consistent with clinical transplant protocols for the frequency of screening potential transplant recipient sera for preformed HLA-specific antibodies.

Interpretative Guidelines §493.1278(d)(4)-(d)(5):

A recipient's antibody profile should be evaluated when the individual is entered on the transplant waiting list. Determine whether the laboratory obtains specimens at initial typing for antibody screening and for pre-transplantation auto crossmatches.

The laboratory should have clearly defined and appropriate screening protocols for potentially sensitizing events such as transfusion, transplant loss, pregnancy or infection. Verify that the laboratory obtains and tests patient specimens to determine if there have been changes in the antibody profiles as defined by the transplant center's protocols. Determine when the laboratory verifies that the antibodies in the serum have been characterized against HLA antigens.

Probes §493.1278(d)(4)-(d)(5)

What policies and procedures has the laboratory implemented in an effort to procure monthly serum specimens for potential transplant recipients?

What is the laboratory's frequency for screening potential transplant recipient sera for preformed HLA-specific antibodies?

D5759

§493.1278 Standard: Histocompatibility.

(d)(6) Check each antibody screening by testing, at a minimum the following:

(d)(6)(i) A positive control material containing antibodies of the appropriate isotype for the assay.

(d)(6)(ii) A negative control material.

Interpretative Guidelines §493.1278(d)(6):

For serologic antibody screening, each tray must include at least one positive control serum previously shown to react with all lymphocytes and one negative control serum which has been demonstrated to be non-cytotoxic or lack antibody. Results are invalid if controls fail to react as expected. Cell viability in the negative control well at the time of reading must be sufficient to permit accurate interpretation of results. Viability should exceed 80%. The positive control must contain antibodies of the appropriate isotype (e.g., IgG and/or IgM). If the frozen cell tray is specific for Class II (HLA-DR or DQ) antibody testing, the laboratory must ensure B cells are being tested and have a mechanism to distinguish Class II antibodies from antibodies to Class I antigens that are also found on B cells.

Laboratories using ELISA and/or flow cytometric techniques must include one positive control serum and one negative control serum. Reagent controls for non-specific binding of antibody should be included with all ELISA testing. The negative control for flow cytometers should demonstrate non-reactivity and the positive control should be specific for HLA antigens. Again, the positive control for both techniques must contain antibodies of the appropriate isotype (i.e., IgG and/or IgM).

Verify that the laboratory uses a negative control and the appropriate isotype for its positive control.

Verify that the laboratory has established acceptability criteria for each control and for each method it uses.

D5761

§493.1278 Standard: Histocompatibility.

(d)(7) As applicable, have available and follow written criteria and procedures for antibody identification to the level appropriate to support clinical transplant protocol.

Probe §493.1278(d)(7):

Does the laboratory's policies specify when antibody reactivity (positive antibody screen) will be further characterized, (i.e., identification of antibody directed against specific HLA antigens) and the procedures to be used for antibody identification?

D5763

§493.1278 Standard: Histocompatibility.

(e) **Crossmatching.** The laboratory must do the following:

(e)(1) Use a technique(s) documented to have increased sensitivity in comparison with the basic complement-dependent microlymphocytotoxicity assay.

Interpretative Guidelines §493.1278(e)(1):

The minimum technique for crossmatching for transplantation must be more sensitive than the basic lymphocytotoxicity test (standard complement dependent or NIH procedure). A technique that enhances sensitivity must be used (e.g., increased incubation time, additional wash steps, antihumanglobulin (AHG) augmentation, ELISA testing, flow cytometry testing).

D5765

§493.1278 Standard: Histocompatibility.

(e)(2) Have available and follow written criteria for the following:

(e)(2)(i) Selecting appropriate patient serum samples for crossmatching.

Interpretative Guidelines §493.1278(e)(2)(i):

The laboratory must have clearly defined protocols for selection of serum for crossmatch testing. There are numerous acceptable protocols for the selection of crossmatch samples which vary from transplant center to center. However, every effort should be made to procure a specimen at the time of transplant or unless the laboratory can clearly establish that the patient did not receive a blood transfusion or other alloimmunizing event between the times of specimen collection and transplant date.

Review patient transplant records for lymphocyte crossmatch results. Verify serum selected for crossmatching against antibody screening/identification records. Verify if the serum is tested at an optimal dilution. Crossmatches are performed with donor T cells (T lymphocytes) or unseparated lymphocytes. Crossmatches with donor B cells (B lymphocytes) may be performed.

Probes §493.1278(e)(2)(i):

Does the laboratory's policies and procedures specify which patient serum samples are to be used for crossmatching (e.g., renal, pancreas, heart, lung, small intestine or liver transplants)?

(e)(2)(ii) The preparation of donor cells or cellular extracts (for example, solubilized antigens and nucleic acids), as applicable to the crossmatch technique(s) performed.

Interpretative Guidelines §493.1278(e)(2)(ii):

There are various techniques for the isolation of donor cells for use in crossmatching e.g., immunomagnetic beads, monoclonal antibody preparations, density gradient (ficoll hypaque). Crossmatching techniques utilizing cellular extracts (solubilized antigens and nucleic acid) are not well documented in the clinical setting.

Determine if the laboratory follows manufacturer's product insert procedures. Use D5479.

Verify that the laboratory has established procedures and criteria for cell preparation viability, purity and quantity (i.e. peripheral blood, lymph node, spleen).

D5767

§493.1278 Standard: Histocompatibility.

(e)(3) Check each crossmatch and compatibility test for HLA Class II antigenic differences using control materials to monitor the test components and each phase of the test system

to ensure acceptable performance.

Interpretative Guidelines §493.1278(e)(3):

The mixed leukocyte (lymphocyte) culture (MLC) is used by a small number of laboratories and it may be used in conjunction with other cellular assays such as cell mediated lympholysis (CML), primed lymphocyte typing (PLT) or homozygous typing cell (HTC) to determine donor recipient pair compatibility in renal or tissue transplants.

The MLC method may vary from micro, macro, one way or both one way, and two way. Data expressed in counts per minute of tritiated thymidine (H3) are used to calculate the stimulation index (SI) or the relative response (RR). Controls include: a negative control (responder cells stimulated with autologous cells), positive controls (responder cells stimulated with cells from unrelated individuals with known Class II antigen differences or fresh or frozen cell pool). If the laboratory performs MLCs, review their criteria for accepting or rejecting a run and a narrative report on donor recipient compatibility. Confirm that all combinations of any given stimulator is tested against any given responder.

Verify that the laboratory has established criteria for defining positive and negative crossmatches.

Example 1:

Basic crossmatch technique: (includes increased incubation time testing or wash(es))

- 1) Each crossmatch tray must include one positive control serum previously shown to react with all cells and one negative control serum which demonstrates non-cytotoxic activity. Additional controls may include antisera against specific cell lines and reagent controls.*
- 2) Each serum is tested undiluted and at one or more dilutions.*

Example 2:

Anti-human globulin augmentation:

- 1) Each crossmatch tray must include one positive control serum previously shown to react with all cells and one negative control serum which demonstrates non-cytotoxic activity. Additional controls may include antisera against specific cell lines and reagent controls.*
- 2) Each serum is tested undiluted and at one or more dilutions.*
- 3) Verify that AHG has been titered for optimum test performance.*

Example 3:

Flow cytometry:

- 1) Each crossmatch must include one positive control serum and one negative control serum. The positive control should be human serum of the appropriate isotype and specific for HLA antigens shown to react with all cells. The negative control should demonstrate non-reactivity against lymphocytes.*
- 2) Verify that the laboratory has established a threshold for determining a positive reaction (e.g., mean channel shifts, quantitative fluorescence measurements).*
- 3) The laboratory should be running an optical standard (lens focusing and alignment) and fluorescent standard (adequate signal amplification) with each use of the instrument.*
- 4) Verify that the laboratory has established an optimum serum/cell ratio (standard number of cells to a fixed volume of serum).*
- 5) A multi color technique should be used to ensure the purity of the cell population being tested.*

Probes §493.1278(e)(3):

What is the laboratory's control acceptance criteria for MLC testing?

D5769

§493.1278 Standard: Histocompatibility

(f) Transplantation. Laboratories performing histocompatibility testing for transfusion and transplantation purposes must do the following:

(f)(1) Have available and follow written policies and protocols specifying the histocompatibility testing (that is, HLA typing, antibody screening, compatibility testing and crossmatching) to be performed for each type of cell, tissue or organ to be transfused or transplanted. The laboratory's policies must include, as applicable--

(f)(1)(i) Testing protocols for cadaver donor, living, living-related, and combined organ and tissue transplants;

(f)(1)(ii) Testing protocols for patients at high risk for allograft rejection; and

(f)(1)(iii) The level of testing required to support clinical transplant protocols (for example, antigen or allele level).

Interpretative Guidelines §493.1278(f):

In conjunction with the transplantation center the laboratory establishes written policies on the testing protocols it performs in support of the clinical transplant program. Policies should address when HLA testing and final crossmatches are required for patients that have demonstrated presensitization. For organs such as liver and heart (non-renal), it is not uncommon for laboratories to perform retrospective crossmatches if the patient demonstrates the absence of preformed antibodies by prior screening. Failure to perform a crossmatch prior to transplant is not a deficiency provided emergency transplant circumstances are documented.

For solid organ transplants (renal, heart, liver, lung, small intestine):

- 1. Determine what tests are performed for potential kidney and pancreas recipients.*
- 2. Determine what tests are performed on living-related or unrelated donors and cadaver donors referred to the laboratory.*
- 3. Determine if the laboratory performs HLA typing using complement dependent lymphocytotoxicity testing (antigen level) and/or DNA testing (allele level);*
- 4. Compare policies for pre-sensitized patients with laboratory antibody screening and identification protocols for consistency;*
- 5. Verify that the laboratory is using a crossmatch technique with increased sensitivity; and*
- 6. Deviations from the established protocols should be documented by the laboratory, indicating the reason for the deviation, e.g., transplant physician request, emergency transplant.*

For transfusions (platelet support of refractory patients):

- 1. Determine what tests are performed on recipients and donors. Recipients are usually HLA-A and HLA-B typed, e.g., platelets do not have Class II (HLA-DR, DQ) antigens on their surface. Donors may be typed by the laboratory, a blood center or a donor program laboratory. HLA typing may be performed using complement dependent lymphocytotoxicity testing (antigen level) and/or DNA testing (allele level).*
- 2. Determine if the laboratory performs antibody screening/identification on the recipient. Compare with the laboratory protocol for antibody screening and identification.*
- 3. Determine if the laboratory performs Class I crossmatch testing.*

For tissue transplant (bone marrow/stem cells, etc.)

- 1. Determine what level of HLA typing is performed on recipients and donors. For bone marrow/stem cell transplantation, recipients are at a minimum HLA-A and HLA-B typed by complement dependent lymphocytotoxicity and/or DNA testing. Recipients should be HLA-DR typed by high resolution DNA typing (allele level). Donors may be typed by the*

laboratory or a donor program laboratory.

2. Determine if the laboratory performs crossmatch testing, when a selected potential donor has an HLA mismatch. Determine if the laboratory performs Class II compatibility to evaluate Class II identity by either MLC testing, high resolution DNA typing, or a family study.

§493.1278(f) Probes:

What is the laboratory's policy/protocol on referring patient specimens for testing at another laboratory?

What is the laboratory's policy/protocol on accepting HLA typing results obtained at another laboratory (i.e., does the laboratory reconfirm (repeat) testing)?

D5771

§493.1278 Standard: Histocompatibility.

(f)(2) For renal allotransplantation and combined organ and tissue transplants in which a kidney is to be transplanted, have available results of final crossmatches before the kidney is transplanted.

Probes §493.1278(f)(2):

If the laboratory performs cadaveric renal transplant testing, what are the staffing policies and how do they ensure 24-hour coverage of qualified testing personnel and supervision for technical review?

D5773

§493.1278 Standard: Histocompatibility.

(f)(3) For nonrenal transplantation, if HLA testing and final crossmatches were not performed prospectively because of an emergency situation, the laboratory must document the circumstances, if known, under which the emergency transplant was performed, and records of the transplant must reflect any information provided to the laboratory by the patient's physician.

§493.1278 Standard: Histocompatibility.

(g) The laboratory must document all control procedures performed, as specified in this section.

§493.1278(g) Guidelines:

All QC records must be maintained for two years including instrument charts, graphs, printouts, transcribed data, manufacturer's assay information sheet for control and calibration materials and reagents to include typing trays, primers and/or probes. Do not dictate the acceptable format for documentation.

D5775

§493.1281 Standard: Comparison of test results.

(a) If a laboratory performs the same test using different methodologies or instruments, or performs the same test at multiple testing sites, the laboratory must have a system that

twice a year evaluates and defines the relationship between test results using the different methodologies, instruments, or testing sites.

Interpretive Guidelines §493.1281(a)-(c):

The laboratory must have a system to monitor and evaluate all testing it performs. Examples of materials that may be used to evaluate the same test performed by different methodologies, at multiple locations, and/or on multiple instruments in the same laboratory are proficiency testing samples, split samples or "blind" testing of materials with known values.

A laboratory that performs the same test at multiple locations or on more than one instrument must have written criteria for acceptable differences in test values (e.g., between different or identical models of an instrument from the same manufacturer, between instruments from different manufacturers).

If the laboratory performs calibration verification as specified in §493.1255(b), it may use the calibration verification to meet the requirements at §493.1281(a), provided the 3 levels of materials used for calibration verification meet the laboratory's criteria for acceptable differences in test values.

D5777

§493.1281 Standard: Comparison of test results.

(b) The laboratory must have a system to identify and assess patient test results that appear inconsistent with the following relevant criteria, when available:

(b)(1) Patient age.

(b)(2) Sex.

(b)(3) Diagnosis or pertinent clinical data.

(b)(4) Distribution of patient test results.

(b)(5) Relationship with other test parameters.

Interpretive Guidelines §493.1281(b):

Verify that the laboratory has a system in place to monitor and evaluate test results for inconsistencies with patient information, and for correlation between test results. For example, a laboratory could multiply the hemoglobin result by a factor of 3, to see if the result is equal to the hematocrit. If the laboratory has auto-validation in its Laboratory Information System (LIS), verify that the laboratory is taking steps to reduce the likelihood of sample-switching errors, for example, when the creatinine result is significantly different from the patient's previous creatinine test results, or if the MCV is significantly different from the patient's previous test results and the patient did not receive a blood transfusion.

For automated laboratories, inconsistent patient results may be evaluated through the use of verified LIS supported logic, patient distribution test results, verified automated test comparison logic programs and individual test repeat criteria.

Probes §493.1281(b):

How does the laboratory obtain sufficient information to enable an evaluation of test results with clinically relevant patient information?

Does the laboratory have procedures to assess and evaluate patient test results for inconsistencies?

For example:

- Hemoglobin and Hematocrit (MCHC value exceeds reference range);
 - BUN and Creatinine comparison;
 - Albumin and Total Protein;
 - Correlation of urine culture with urine microscopic; and
 - Alkaline phosphatase with orthopedic surgical patients and/or pediatric patients; and
 - Correlation of microscopic sediment findings with macroscopic results, such as, the presence of protein with casts, positive occults blood with red cells, and positive leukocyte esterase with white cells.
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§493.1281 Standard: Comparison of test results.

(c) The laboratory must document all test result comparison activities.

Interpretive Guidelines §493.1281(c):

The actual measurement(s) of test results and comparison activities must be recorded. Acceptable formats for documentation may vary. Cite documentation deficiencies at §493.1281(a) or §493.1281(b). Use D5775 or D5777, as appropriate.

D5779

§493.1282 Standard: Corrective actions.

(a) Corrective action policies and procedures must be available and followed as necessary to maintain the laboratory's operation for testing patient specimens in a manner that ensures accurate and reliable patient test results and reports.

Interpretive Guidelines §493.1282(a):

Corrective action must be taken when unacceptable differences in test values occur with testing performed using different methodologies or instruments or with the same test performed at multiple testing sites.

Probes §493.1282(a):

When test results do not correlate with patient information (e.g., age, sex, submitted diagnosis) what actions are taken by the laboratory to confirm test results or patient information?

D5781

§493.1282 Standard: Corrective actions.

(b) The laboratory must document all corrective actions taken, including actions taken when any of the following occur:

(b)(1) Test systems do not meet the laboratory's verified or established performance specifications, as determined in §493.1253(b), which include but are not limited to--

(b)(1)(i) Equipment or methodologies that perform outside of established operating parameters or performance specifications;

(b)(1)(ii) Patient test values that are outside of the laboratory's reportable range of test results for the test system; and

(b)(1)(iii) When the laboratory determines that the reference intervals (normal values) for a test procedure are inappropriate for the laboratory's patient population.

Interpretive Guidelines §493.1282(b)(1):

The laboratory's corrective action records should contain sufficient information to resolve the problem if it reoccurs.

Probes §493.1282(b)(1):

When equipment malfunctions or a test method problem exists, how does the laboratory identify and solve the problem?

What corrective actions are taken if patient test results exceed the laboratory's reportable range of patient test results?

If a dilution procedure is used when patient results exceed the test system's reportable range, how does the laboratory assure the appropriate diluent is used for each type of specimen? Use D5401.

How does the laboratory verify and document the accuracy of the results for diluted specimens? Use D5421 or D5423 as appropriate.

D5783

§493.1282 Standard: Corrective actions.

(b)(2) Results of control or calibration materials, or both, fail to meet the laboratory's established criteria for acceptability. All patient test results obtained in the unacceptable test run and since the last acceptable test run must be evaluated to determine if patient test results have been adversely affected. The laboratory must take the corrective action necessary to ensure the reporting of accurate and reliable patient test results.

Interpretive Guidelines §493.1282(b)(2):

When an internal control fails to fall within the defined limits of acceptability, the laboratory must identify the reason for the failure and correct the problem before resuming testing of patients. The laboratory must evaluate all patients test results since the last acceptable external control.

Probes §493.1282(b)(2):

When suboptimal staining or improper coverslipping are identified through quality control procedures, what corrective actions does the laboratory take?

What actions does the laboratory take when controls reflect an unusual trend or are outside of the acceptable limits and other means of assessing and correcting unacceptable control values have failed to identify and correct the problem?

D5785

§493.1282 Standard: Corrective actions.

(b)(3) The criteria for proper storage of reagents and specimens, as specified under §493.1252(b), are not met.

Probes §493.1282(b)(3):

What actions does the laboratory take if the storage temperature for a test system's reagents has been exceeded?

D5787

§493.1283 Standard: Test records.

- (a) The laboratory must maintain an information or record system that includes the following:
- (a)(1) The positive identification of the specimen.
 - (a)(2) The date and time of specimen receipt into the laboratory.
 - (a)(3) The condition and disposition of specimens that do not meet the laboratory's criteria for specimen acceptability.
 - (a)(4) The records and dates of all specimen testing, including the identity of the personnel who performed the test(s).

Interpretive Guidelines §493.1283(a):

The regulations provide laboratories the flexibility to establish a system that ensures positive patient identification through specimen accessioning and storage, testing and reporting of test results. This may include a system that involves labeling the specimen container and request slip or the patient's medical record or chart with a unique patient identification number, but does not preclude the use of other mechanisms to assist in patient identification and tracking of specimens throughout the testing and reporting processes. The patient's name may be used as part of the identification system.

Ensure that work records reflect all the tests and dates of performance of in-house patient testing. For example, in bacteriology, each step from media inoculation to organism isolation and identification must be documented on worksheet records either manually or in a computer system.

Corrections of laboratory results include the corrected result, incorrect result (noted as such), the date of the correction, and the initials of the person making the correction. Laboratory records should not be documented in pencil and the use of whiteout is not acceptable for making corrections.

Probes §493.1283(a):

Do the records reflect all patient testing and the dates of their performance?

If handwritten values were reported, can the laboratory demonstrate the analytic source of those results?

If the laboratory has not retained the appropriate test records, cite D3031, D3033, or D3035.

D5789

§493.1283 Standard: Test records.

- (b) Records of patient testing including, if applicable, instrument printouts, must be retained.

Interpretative Guidelines §493.1283(b):

The regulations do not require that instrument printouts be posted directly in the patient's medical record or chart. However, these printouts must be maintained as part of the laboratory's record retention requirements specified throughout the regulations.

Probes §493.1283(b):

Are the original analytic work records complete (e.g., in a randomly chosen sample, is there an instrument printout for every day of the month on which testing was performed)?
Are the original, as opposed to transcribed and/or edited work records, being retained?
If the laboratory fails to retain the records for the appropriate amount of time, use D3031.

D5791

§493.1289 Standard: Analytic systems quality assessment.

(a) The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess, and when indicated, correct problems identified in the analytic systems specified in §§493.1251 through 493.1283.

Interpretative Guidelines §493.1289(a)-(c):

Quality Assessment (QA) is an ongoing review process that encompasses all facets of the laboratory's technical and non-technical functions at all location/sites where testing is performed. QA also extends to the laboratory's interactions with and responsibilities to patients, physicians, and other laboratories ordering tests, and the non-laboratory areas or the facility of which it is a part.

When the laboratory discovers an error or identifies a potential problem, actions must be taken to correct the situation. This correction process involves identification and resolution of the problem, and development of policies that will prevent recurrence. Policies for preventing problems that have been identified must be written as well as communicated to the laboratory personnel and other staff, clients, etc., as appropriate. Over time, the laboratory must monitor the corrective action(s) to ensure the action(s) taken have prevented recurrence of the original problem.

All pertinent laboratory staff must be involved in the assessment process through discussions or active participation.

QA of the Analytic System includes assessing:

- *Test procedures;*
- *Accurate and reliable test systems, equipment, instruments, reagents, materials, and supplies;*
- *Specimen and reagent storage condition;*
- *Equipment/instrument/test/system maintenance and function checks;*
- *Establishment and verification of method performance specifications;*
- *Calibration and calibration verification;*
- *Control procedures;*
- *Comparison of test results;*
- *Corrective actions; and*
- *Test records.*

For Clinical Cytogenetics, cases, the laboratory should identify increases in or excessive culture failure rates, determine the contributing factors, document efforts to reduce or eliminate these factors and assess the effectiveness of actions taken. (i.e., a decrease in the culture failure rate).

Review assessment policies, procedures and reports to verify that the laboratory has a system in place to ensure continuous improvement. Corrective action reports are one indication that the laboratory is monitoring and evaluating laboratory performance and the quality of services.

Select a sample of abnormal cytology patient reports and determine that, when available, the histopathology and cytology comparison was performed and the cytology 5-year retrospective review was performed. Ensure the laboratory documents any discrepancies and performs corrective action.

Review quality control records to determine if the laboratory's monitoring efforts are detecting control failures, shifts, and trends. If the surveyor identifies previously undetected quality control failures or omission, then the laboratory's system for monitoring and evaluating quality control may not be adequate.

For International Normalized Ratio (INR) calculation, ensure the laboratory:

- Periodically verifies, for each thromboplastin lot number in use, the correct normal prothrombin time mean and (the International Sensitivity Index (ISI) value are being used for calculating the INR value.
- Periodically verifies the accuracy of the INR calculation (manual, instrument or LIS).

To verify Prothrombin time testing with INR calculations:

- Check the accuracy of normal Prothrombin time mean calculation (manual, instrument or LIS).
- Verify the ISI used in the calculation correlates with the ISI specified in the reagent package insert. Select an abnormal low or abnormal high prothrombin time result and verify the calculation.

Probes §493.1289(a):

For clinical cytogenetics cases, does the laboratory monitor the frequency of culture failures and sub-optimal analyses?

Does the laboratory add additional maintenance procedures and/or function checks, when needed, to ensure accurate and reliable test results?

What is the laboratory's system for monitoring and evaluating test results for inconsistencies with patient information?

D5793

§493.1289 Standard: Analytic systems quality assessment.

(b) The analytic systems quality assessment must include a review of the effectiveness of corrective actions taken to resolve problems, revision of policies and procedures necessary to prevent recurrence of problems, and discussion of analytic systems quality assessment reviews with appropriate staff.

Interpretative Guidelines §493.1289(b):

Verify that the laboratory has a system in place to monitor and evaluate test results for inconsistencies with patient information, and for correlation between test results. For example, a laboratory could multiply the hemoglobin result by a factor of 3, to see if the result is equal to the hematocrit. If the laboratory has auto-validation in its Laboratory Information System (LIS), verify that the laboratory is taking steps to reduce the likelihood of sample-switching errors, for example, when the creatinine result is significantly different from the patient's previous creatinine test results, or if the MCV is significantly different from the patient's previous test results and the patient did not receive a blood transfusion.

Probes §493.1289(b):

How does the laboratory address multiple failed or sub-optimal cultures that have been submitted from one client?

How does the laboratory use the review of all normal or negative gynecologic specimens received within the previous 5 years to assess the analytic system and communicate findings to the staff?

(c) The laboratory must document all analytic systems assessment activities.

Interpretive Guidelines §493.1289(c):

The steps taken by the laboratory to identify and correct problems and prevent their recurrence must be documented. All laboratory policies amended due to its QA activities must also be noted.

D5800

Postanalytic Systems

§493.1290 Condition: Postanalytic systems.

Each laboratory that performs nonwaived testing must meet the applicable postanalytic systems requirements in §493.1291 unless HHS approves a procedure, specified in Appendix C of the State Operations Manual (CMS Pub. 7) that provides equivalent quality testing. The laboratory must monitor and evaluate the overall quality of the postanalytic systems and correct identified problems as specified in §493.1299 for each specialty and subspecialty of testing performed.

Interpretive Guidelines §493.1290:

Significant deficiencies cited under this condition may indicate deficiencies under personnel responsibilities. Use D5800 when deficiencies are identified that are: significant and have the potential to, or adversely affect, patient testing, are systemic and pervasive throughout the laboratory, and are not limited to any one specialty or subspecialty.

D5801

§493.1291 Standard; Test report.

(a) The laboratory must have an adequate manual or electronic system(s) in place to ensure test results and other patient-specific data are accurately and reliably sent from the point of data entry (whether interfaced or entered manually) to final report destination, in a timely manner. This includes the following:

Interpretive Guidelines §493.1291(a):

The regulations apply to manual as well as automated record systems, i.e., a laboratory information system or LIS. However, the regulations do not specify the mechanism or frequency for which a laboratory should evaluate its record storage and retrieval system(s).

Probes §493.1291(a):

How does the laboratory ensure that transmitted reports are legible and the information received at the final destination was the same data sent by the laboratory?

If the laboratory uses a LIS or facsimile, what security measures have been instituted to ensure that transmitted reports go directly from the device sending reports only to the authorized individual, their location or electronic system?

§493.1291 Standard: Test report.

(a)(1) Results reported from calculated data.

(a)(2) Results and patient-specific data electronically reported to network or interfaced systems.

(a)(3) Manually transcribed or electronically transmitted results and patient-specific information reported directly or upon receipt from outside referral laboratories, satellite or point-of-care testing locations.

Interpretive Guidelines §493.1291(a)(3):

Manually transcribed or electronically transmitted results from an outside referral laboratory or from within the laboratory system (e.g., satellite or point-of-care testing locations) must be periodically verified for accuracy and timely reporting.

D5803

§493.1291 Standard: Test report.

(b) Test report information maintained as part of the patient's chart or medical record must be readily available to the laboratory and to CMS or a CMS agent upon request.

Interpretive Guidelines §493.1291(b):

The test report information should be legible, understandable, and complete.

D5805

§493.1291 Standard: Test report.

(c) The test report must indicate the following:

(c)(1) For positive patient identification, either the patient's name and identification number, or a unique patient identifier and identification number.

Interpretive Guidelines §493.1291(c)(1)- (c)(6):

Use D5203 for deficiencies related to specimen identification problems.

When used on the test report, the patient's name must be accompanied by an identification or accession number. When for confidentiality purposes a patient's name is not used or when the identity of the person is not known, a unique patient identifier and identification or accession number must be used on the report.

(c)(2) The name and address of the laboratory location where the test was performed.

Interpretive Guidelines §493.1291(c)(2):

Laboratories having a single certificate for multiple sites/locations must have a system in place to identify which tests were performed at each site.

A code to identify the name and address of the laboratory performing testing is acceptable as long as the code is clearly annotated on the patient test report. This may be accomplished by using abbreviated indicators (e.g., asterisks) as long as they are identified and apparent to the individual receiving the report. This or a similar system

may be seen on cumulative reports. The name and address of the reference laboratory may also be defined on a subsequent page or on the back of the report. Laboratories have latitude to develop other formats to meet this requirement.

§493.1291 Standard: Test report.

(c)(3) The test report date.

Interpretive Guidelines §493.1291(c)(3):

The date of the test report is the date results were generated as a final report and must not change on copies generated at a later date.

(c)(4) The test performed.

Interpretive Guidelines §493.1291(c)(4):

Laboratories using manufacturer's instruments, kits or test systems labeled for "investigational use only" or "research use only" must clearly state that the test results are not to be used for treatment or diagnostic purposes. If results of such tests are being reported without a disclaimer statement, or are being used by the provider for patient care, they are in the same category as in-house developed tests and the laboratory must establish performance specifications in accordance with §493.1253.

The disclaimer for Analyte Specific Reagents (ASR) should state ["This test was developed and its performance characteristics determined by (Laboratory Name). It has not been cleared or approved by the U.S. Food and Drug Administration"]. The ASR disclaimer on the test report is required by the FDA under 21 CFR, Part 809.30 "Restrictions on the sale, distribution and use of analyte specific reagents."

(c)(5) Specimen source, when appropriate.

Interpretive Guidelines §493.1291(c)(5):

Some examples of source of the specimen needed by the laboratory to accurately perform testing and report results would be: site of culture; type of body fluid; whether a submitted separated specimen is plasma, serum, urine, etc.

§493.1291 Standard: Test report.

(c)(6) The test result and, if applicable, the units of measurement or interpretation, or both.

Interpretive Guidelines §493.1291(c)(6):

If the laboratory prints normal ranges on the patient test report, verify that "sex and/or age specific" normal ranges are printed by the LIS on the patient test report.

"Less than" is used for reporting test results (qualitative or quantitative) that are below the laboratory's detection limits for an analyte. (Detection limits must be established through method verification as described in §493.1253.) "Equivalent designation" is used to report test results for those methods that yield results below a clinically significant level (e.g., for a quantitative immunology test, patient results may be clinically negative at a 1:8 titer and test results may be reported as "1:8 negative". The normal range is 1:8 or less.) "Greater than" is used for reporting test results (qualitative or quantitative) that are above the laboratory's detection limits for an analyte. If patient test results exceed the laboratory's reportable range, the laboratory must report the result as greater than the highest detection limit, reassay a diluted patient specimen and report the calculated result, or send the specimen to a reference laboratory.

For flow cytometry, to interpret results, staff should have access to the complementary

clinical picture of the patient. This may include such results as white cell count, cell differential, cell morphology, and cytogenetics.

Flow cytometry patient data files should include any gating analysis regions used to obtain reported test results.

For genetic tests, the laboratory should include the test method(s) employed and any mutations on the test report.

Probes §493.1291(c)(6):

When additional information is critical for the interpretation of test results (e.g., screening vs. confirmatory procedures), how does the laboratory convey this information to the individual ordering or using test results?

If the laboratory does not print normal ranges on the test report, how does the laboratory notify the client that reported results are abnormal for the patient due to their particular sex and/or age?

§493.1291 Standard: Test report.

(c)(7) Any information regarding the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability.

Interpretive Guidelines §493.1291(c)(7):

If the laboratory functions as a reference laboratory, how does it notify the referring laboratory or client of unacceptable specimens in a timely manner? Use D5801 to cite timeliness deficiencies. Use D5805 to cite the referring laboratory's failure to notify the appropriate individual concerning the unacceptable specimen.

D5807

§493.1291 Standard: Test report

(d) Pertinent "reference intervals" or "normal" values, as determined by the laboratory performing the tests, must be available to the authorized person who ordered the tests and, if applicable, the individual responsible for using the test results.

Interpretive Guidelines §493.1291(d):

The laboratory must ensure the "reference intervals" or "normal" values it provides to its clients are accurate, include appropriate units of measurement, and reflect the method performed and the patient population (if applicable).

D5809

§493.1291 Standard: Test report.

(e) The laboratory must, upon request, make available to clients a list of test methods employed by the laboratory and, as applicable, the performance specifications established or verified as specified in §493.1253. In addition, information that may affect the interpretation of test results, for example test interferences, must be provided upon request. Pertinent updates on testing information must be provided to clients whenever changes occur that affect the test results or interpretation of test results.

Interpretive Guidelines §493.1291(e):

When the laboratory changes methods, establishes a new procedure or refers tests to

another laboratory, the laboratory must provide the client with necessary updated information concerning parameters such as patient preparation, preservation of specimens, specimen collection or new "normal" values.

§493.1291(e) Probes:

How does the laboratory keep its clients informed about tests offered, methods used, and specimen requirements?

What means does the laboratory use to provide interpretation of results to its clients?

D5811

§493.1291 Standard: Test report.

(f) Test results must be released only to authorized persons and, if applicable, the individual responsible for using the test results and the laboratory that initially requested the test.

Probes §493.1291(f):

What security measures have been instituted to ensure that reports go directly from the device sending reports (e.g., LIS, facsimile) to only the individual ordering the test or utilizing the test results?

D5813

§493.1291 Standard: Test report.

(g) The laboratory must immediately alert the individual or entity requesting the test and, if applicable, the individual responsible for using the test results when any test result indicates an imminently life-threatening condition, or panic or alert values.

Interpretive Guidelines §493.1291(g):

The laboratory records should document the date, time, test results, and person to whom the test results were reported.

Probes §493.1291(g):

What means does the laboratory use to ensure the person ordering a test or the caregiver is alerted in a timely manner to critical or panic test results?

D5815

§493.1291 Standard: Test report.

(h) When the laboratory cannot report patient test results within its established time frames, the laboratory must determine, based on the urgency of the patient test(s) requested, the need to notify the appropriate individual(s) of the delayed testing.

Interpretive Guidelines §493.1291(h):

If a delay in reporting patient test results may negatively impact patient care, the laboratory should have an alternative method for reporting patient results when the LIS or test system is down.

Cite deficiencies only when the laboratory has failed to notify its client(s) when delays in

testing patient specimens have the potential for or are adversely affecting patient care.

Probes §493.1291(h):

What criteria has the laboratory established for notifying the appropriate individual of the delay in testing? Use D5403.

How will the laboratory report patient test results if the LIS or test system is down?

D5817

§493.1291 Standard: Test report.

(i) If a laboratory refers patient specimens for testing--

(i)(1) The referring laboratory must not revise results or information directly related to the interpretation of results provided by the testing laboratory;

Interpretive Guidelines §493.1291(h)(i)(1):

If the laboratory transcribes results from the reference laboratory report, the test results, interpretation and information directly related to the interpretation must be copied exactly as reported by the reference laboratory. The report must adhere to the requirements in §§493.1291(c)(1)–(c)(7) and 493.1291(d).

(i)(2) The referring laboratory may permit each testing laboratory to send the test result directly to the authorized person who initially requested the test. The referring laboratory must retain or be able to produce an exact duplicate of each testing laboratory's report; and

Interpretive Guidelines §493.1291(h)(i)(2):

An "exact duplicate" is an exact copy of the information sent to the individual requesting the test or using the test result(s), and includes the name and address of the laboratory performing the test. The exact copy need not be paper, it may be retrieved from a computer system, microfilm or microfiche record, as long as it contains the exact information in the same format as sent to the individual ordering the test or utilizing the test results. For tests requiring an authorized signature or containing personnel identifiers (e.g., Pathology), the exact duplicate must include the signatures or identifiers. "Pathology" includes all of its subspecialties (i.e., Histopathology, Oral pathology, Cytology).

A "preliminary report" means a test result that has been reported to the authorized person or laboratory that initially requested the test before the final test result is completed. Frequently, a preliminary report will contain significant, but not definitive information (e.g., a urine culture preliminary report of >100,000 Gram-negative bacilli after 24 hours incubation or a beta subunit preliminary report of >200 miu/ml). It should be noted on the report when the result is a preliminary result and that a final report will follow.

A "partial report" means multiple tests are ordered on the same specimen or patient. If partial reports are issued for only those tests that have been completed, then the report date will be the date when all tests have been completed. However, the laboratory should be able to identify the date that each new test is appended to the report.

The laboratory must have a system for retaining copies of all reports including original, preliminary, corrected, and final reports. This includes computer-generated reports.

(i)(3) The authorized person who orders a test must be notified by the referring laboratory of the name and address of each laboratory location where the test was performed.

Interpretive Guidelines §493.1291(h)(i)(3):

Test report forms may include codes to identify the name and address of the laboratory that performed the test, provided the interpretations of the codes are available to the authorized person using the test results.

D5819

§493.1291 Standard: Test report.

(j) All test reports or records of the information on the test reports must be maintained by the laboratory in a manner that permits ready identification and timely accessibility.

D5821

§493.1291 Standard: Test report.

(k) When errors in the reported patient test results are detected, the laboratory must do the following:

(k)(1) Promptly notify the authorized person ordering the test and, if applicable, the individual using the test results of reporting errors.

Interpretive Guidelines §493.1291(k)(1):

When determining whether the laboratory gave prompt notification of test and/or reporting errors to the authorized person(s) consider:

- When the error was identified and when the authorized person was notified; and
- Extent of error (e.g., clinically significant results reported on the wrong patient).

Probes §493.1291(k)(1):

What mechanism(s) does the laboratory use for notifying the authorized person of the corrected values?

§493.1291 Standard: Test report.

(k)(2) Issue corrected reports promptly to the authorized person ordering the test and, if applicable, the individual using the test results.

Interpretive Guidelines §493.1291(k)(2):

Corrected reports must clearly indicate that they are corrected reports and the corrected result must also be indicated. Use D5821. For corrected reports in Cytology, use D5659.

How does the laboratory ensure that incorrect original results are not reissued verbally, in writing or electronically?

§493.1291 Standard: Test report.

(k)(3) Maintain duplicates of the original report, as well as the corrected report.

Interpretive Guidelines §493.1291(k)(3):

The laboratory must have a system for maintaining copies of the original and corrected reports. Computer-generated reports or electronically stored copies are acceptable.

Copies of all reports, including corrected reports, provided by the referral laboratory must be maintained by both the referral and referring laboratories for the required time periods.

Probes §493.1291(k)(3):

For laboratories that maintain the patient's medical record as the test reports, what is the mechanism for differentiating between the incorrect original report and the corrected report?

D5891

§493.1299 Standard: Postanalytic systems quality assessment.

(a) The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess and, when indicated, correct problems identified in the postanalytic systems specified in §493.1291.

Interpretive Guidelines §493.1299(a)-(c):

Quality Assessment (QA) is an ongoing review process that encompasses all facets of the laboratory's technical and non-technical functions and all locations/sites where testing is performed. QA also extends to the laboratory's interactions with and responsibilities to patients, physicians, and other laboratories ordering tests, and non-laboratory areas or departments of the facility of which it is a part.

When the laboratory discovers an error or identifies a potential problem, actions must be taken to correct the situation. This correction process involves investigation, identification and resolution of the problem, and development of policies that will prevent recurrence. Policies for preventing problems that have been identified must be written as well as communicated to the laboratory personnel and other staff, clients, etc., as appropriate. Over time, the laboratory must monitor the corrective action(s) to ensure the action(s) taken have prevented recurrence of the original problem.

All pertinent laboratory staff must be involved in the assessment process through discussions or active participation.

*QA of the **Postanalytic System** includes assessing practices/issues related to test reports. Examples include monitoring and evaluating the accuracy and completeness of the laboratory's test reports (i.e., patient information, test results, normal ranges, and the disposition of unacceptable specimens), and the laboratory's turn-around times and procedures for notification of test results e.g., routine tests, STATS, abnormal or panic values.*

Review a cross-section of patient test reports for accuracy of patient information, test results and normal ranges to verify that the laboratory is effectively monitoring and evaluating the quality and accuracy of the information supplied to its clients.

Verify that the laboratory has a system in place to monitor and evaluate its established reporting time frames and procedures for notification of test results, routine tests, STATS, abnormal or panic values.

If the laboratory uses an LIS, the laboratory must have a mechanism to periodically verify the accuracy of:

- *its calculated data;*
- *its results sent to interfaced systems; and*
- *patient specific data.*

D5893

§493.1299 Standard: Postanalytic systems quality assessment.

(b) The postanalytic systems quality assessment must include a review of the effectiveness of corrective actions taken to resolve problems, revision of policies and procedures necessary to prevent recurrence of problems, and discussion of postanalytic systems quality assessment reviews with appropriate staff.

Interpretive Guidelines §493.1299(b):

Review assessment policies, procedures and reports to verify that the laboratory has a system in place to ensure continuous improvement. Corrective action reports are one indication that the laboratory is monitoring and evaluating laboratory performance and the quality of services.

(c) The laboratory must document all postanalytic systems quality assessment activities.

Interpretive Guidelines §493.1299(c):

The steps taken by the laboratory to identify and correct problems, and prevent their recurrence must be documented. All laboratory policies amended due to its QA activities must be noted.

Probes §493.1299(a)-(c):

What mechanism does the laboratory use to update and correlate the information to clients (e.g., client reference manuals), procedure manuals, reporting systems (e.g., LIS) when the laboratory introduces a new test system with different normal/reference range?

**Subpart K--Quality System for Nonwaived Testing
(Rev. 32, 02-13-2004)**

§493.1200 Introduction.

(a) Each laboratory that performs nonwaived testing must establish and maintain written policies and procedures that implement and monitor a quality systems for all phases of the total testing process (that is, preanalytic, analytic, and postanalytic) as well as general laboratory systems.

(b) The laboratory's quality systems must include a quality assessment component that ensures continuous improvement of the laboratory's performance and services through ongoing monitoring that identifies, evaluates and resolves problems.

(c) The various component of the laboratory's quality system are used to meet the requirements in this part and must be appropriate for the specialties and subspecialties of testing the laboratory performs, services it offers, and clients it serves.

D5002

§493.1201 Condition: Bacteriology.

If the laboratory provides services in the subspecialty of Bacteriology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1261, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1201

Tests or procedures to detect an antigen are categorized in this subspecialty where the antigen is detected or identified. For example, tests or procedures for identifying Group A Streptococcus are categorized in Bacteriology.

D5004

§493.1202 Condition: Mycobacteriology.

If the laboratory provides services in the subspecialty of Mycobacteriology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1262, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1202

Tests or procedures to detect an antigen are categorized in the subspecialty where the antigen is detected or identified. For example, the procedures to identify Mycobacteria are categorized in Mycobacteriology.

D5006

§493.1203 Condition: Mycology.

If the laboratory provides services in the subspecialty of Mycology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1263, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1203

Tests or procedures to detect an antigen are categorized in the subspecialty where the antigen is detected or identified. For example, tests for the identification of fungi are categorized in Mycology.

D5008

§493.1204 Condition: Parasitology.

If the laboratory provides services in the subspecialty of Parasitology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1264, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1204

Tests or procedures to identify an antigen are categorized in the subspecialty where the antigen is detected or identified. For example, procedures to identify a parasite are categorized in the subspecialty of Parasitology; however, procedures to detect or identify an antibody to the parasite are categorized in the subspecialty of General Immunology.

D5010

§493.1205 Condition: Virology.

If the laboratory provides services in the subspecialty of Virology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1265, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1205

Tests or procedures to identify the virus (antigen) are categorized in the subspecialty when the antigen is detected or identified. For example, tests or procedures to detect herpes are categorized in the subspecialty of Virology. Tests or procedures to detect antibodies to Herpes are categorized in the subspecialty of General Immunology.

D5012

§493.1207 Condition: Syphilis serology.

If the laboratory provides services in the subspecialty of Syphilis serology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1207

Quality control requirements for Syphilis Serology are found in §493.1256. Use D5441 through D5485 as appropriate.

D5014

§493.1208 Condition: General immunology.

If the laboratory provides services in the subspecialty of General immunology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1208

Tests or procedures to detect or identify antibodies to a bacteria, virus, parasite, etc., are categorized under the subspecialty of General Immunology. Quality control requirements for General Immunology are found at §493.1256.

D5016

§493.1210 Condition: Routine chemistry.

If the laboratory provides services in the subspecialty of Routine chemistry, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1267, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1210

Quality control requirements for Routine Chemistry are found in §§493.1256 and 493.1267. Use D5441 through D5485 and D5535 through D5539, as appropriate.

D5018

§493.1211 Condition: Urinalysis.

If the laboratory provides services in the subspecialty of Urinalysis, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1211

Quality control requirements for the subspecialty of Urinalysis are found in §493.1256. Use D5441 through D5485, as appropriate.

D5020

§493.1212 Condition: Endocrinology.

If the laboratory provides services in the subspecialty of Endocrinology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1212

Quality control requirements for the subspecialty of Endocrinology are found in §493.1256. Use D5441 through D5485, as appropriate.

D5022

§493.1213 Condition: Toxicology.

If the laboratory provides services in the subspecialty of Toxicology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1213

Quality control requirements for the subspecialty of Toxicology are found in §493.1256. Use D5441 through D5485, as appropriate.

D5024

§493.1215 Condition: Hematology.

If the laboratory provides services in the specialty of Hematology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1269, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1215

Quality control requirements for the subspecialty of automated Hematology are found in §493.1256. Use D5441 through D5485, as appropriate.

D5026

§493.1217 Condition: Immunohematology.

If the laboratory provides services in the specialty of Immunohematology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1271, and §§493.1281 through 493.1299.

D5028

§493.1219 Condition: Histopathology.

If the laboratory provides services in the subspecialty of Histopathology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1273, and §§493.1281 through 493.1299.

D5030

§493.1220 Condition: Oral pathology.

If the laboratory provides services in the subspecialty of Oral pathology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

D5032

§493.1221 Condition: Cytology.

If the laboratory provides services in the subspecialty of Cytology, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1274, and §§493.1281 through 493.1299.

D5034

§493.1225 Condition: Clinical cytogenetics.

If the laboratory provides services in the specialty of Clinical cytogenetics, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1276, and §§493.1281 through 493.1299.

D5040

§493.1226 Condition: Radiobioassay.

If the laboratory provides services in the specialty of Radiobioassay, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, and §§493.1281 through 493.1299.

Interpretative Guidelines §493.1226

Quality control requirements for the subspecialty of Radiobioassay are found in §493.1256. Use D5441 through D5485, as appropriate.

D5042

§493.1227 Condition: Histocompatibility.

If the laboratory provides services in the specialty of Histocompatibility, the laboratory must meet the requirements specified in §§493.1230 through 493.1256, §493.1278, and §§493.1281 through 493.1299.

D5200

General Laboratory Systems

§493.1230 Condition: General laboratory systems.

Each laboratory that performs nonwaived testing must meet the applicable general laboratory systems requirements in §§493.1231 through 493.1236, unless HHS approves a procedure, specified in Appendix C of the State Operations Manual #7, that provides equivalent quality testing. The laboratory must monitor and evaluate the overall quality of the general laboratory systems and correct identified problems specified in §493.1239 for each specialty and subspecialty of testing performed.

Interpretative Guidelines §493.1230

Significant deficiencies cited under this condition may indicate deficiencies under personnel responsibilities. Use D5200 when significant deficiencies are identified and have the potential to, or adversely affect patient testing, are systemic and pervasive throughout the laboratory, and are not limited to any one specialty or subspecialty.

The requirements in this section address those general operational functions that are not specific to any one specialty or subspecialty.

D5201

§493.1231 Standard: Confidentiality of patient information.

The laboratory must ensure confidentiality of patient information throughout all phases of the total testing process that are under the laboratory's control.

Probes §493.1231

How does the laboratory "control" visitor access to the laboratory areas where patient information may be easily viewed (e.g., computer terminals, facsimile machines, worksheets)?

Are there safeguards in place to ensure confidentiality of patient information and test reports? For example, are unauthorized users prohibited from gaining entry?

How does the laboratory ensure its record storage system(s) is secure?

D5203

§493.1232 Standard: Specimen identification and integrity.

The laboratory must establish and follow written policies and procedures that ensure positive identification and optimum integrity of a patient's specimen from the time of collection or receipt of the specimen through completion of testing and reporting of results.

Interpretative Guidelines §493.1232

The regulation provides laboratories the flexibility to establish a system that ensures positive patient identification through specimen collection, labeling, accessioning, processing, (e.g., aliquotting), storage, testing, and reporting of results. Review the laboratory's system (policy and practices) for ensuring positive patient identification from specimen collection through reporting of results.

Optimum integrity of a patient's specimen should be determined according to the test methodology utilized by the laboratory. Review manufacturer's instructions for performance of each test method to ensure the specimen is appropriate for the test system, is stored properly (e.g., maintained at room temperature, kept on ice, separated and frozen or refrigerated), and analyzed within the limitations of the test methodology.

The laboratory must have a procedure to ensure that special handling of specimens is maintained throughout the testing process when necessary, (e.g., GC cultures and GC/Chlamydia probes, blood gas specimens, and DNA probes.)

Probes §493.1232

How does the laboratory ensure positive identification of patient specimens through all phases of testing, especially when similar patient identification information (e.g., address, sex, names, timed specimens, and birth dates) exists?

How does the laboratory assure that special handling of specimens (when specified by the testing laboratory) is maintained throughout the testing process?

Does the laboratory process patient specimens using separate (distinct) or unique identifiers in order to avoid mislabeling, specimen mix-ups, incorrect test request entry, and incorrect reporting of results?

D5205

§493.1233 Standard: Complaint investigations.

The laboratory must have a system in place to ensure that it documents all complaints and problems reported to the laboratory. The laboratory must conduct investigations of complaints, when appropriate.

Interpretative Guidelines §493.1233

Verify that the laboratory documents all complaints and problems reported to the laboratory, and has a mechanism to determine which complaints require investigation.

For Immunochemistry complaints related to transfusion reaction investigation, use D3130 or D5559, as appropriate.

Probes §493.1233

What mechanism does the laboratory have that allows individuals to report complaints or problems to the laboratory?

Does the laboratory have a mechanism to refer complaints or problems to its reference laboratory(s), or other offices or agencies, when appropriate? Does the laboratory document this activity?

D5207

§493.1234 Standard: Communications.

The laboratory must have a system in place to identify and document problems that occur as a result of a breakdown in communication between the laboratory and an authorized person who orders or receives test results.

Interpretative Guidelines §493.1234

Communication may begin with the test request of information requested concerning patient specimens. If the laboratory does not receive the appropriate specimen or patient information needed to perform the tests, the laboratory should assess the information concerning patient preparation and specimen handling requirements provided to the authorized individuals.

The test report form should be easily understood and accurately portray patient test results and other information necessary for interpreting test results (e.g., failure to identify peak and trough).

D5209

§493.1235 Standard: Personnel competency assessment policies.

As specified in the personnel requirements in subpart M, the laboratory must establish and follow written policies and procedures to assess employee and, if applicable, consultant competency.

Interpretative Guidelines §493.1235

Refer to §§493.1413(b)(8) and 493.1451(b)(8) for specific testing personnel competency requirements and refer to §493.1407(e)(12) and §493.1445(e)(13) for establishing policies to monitor each individual's competency and identify remedial training or continuing education needs. Cite deficiencies at this location when the laboratory has developed but is not following personnel competency policies and procedures for technical and clinical consultants, technical supervisors and other laboratory staff.

For microscopic urinalysis, the laboratory must have a system that ensures all personnel report microscopic morphologic data on patient samples in a similar fashion. For initial accuracy, as well as consistency in serial samples from the same patient, the laboratory should assess its staff for consistency with respect to morphologic classification.

Suggested methods include:

- *Circulation of preserved urine sediments with leukocytes, erythrocytes, casts, bacteria, yeast, etc.*

- Use of multi-headed microscopes
- Use of urine sediment photomicrographs

Probes §493.1235

How does the laboratory evaluate the competency of its employees?

If the laboratory uses non-testing personnel to perform preanalytic functions how does it ensure their competency?

If a laboratory utilizes a consultant, how does the laboratory determine if the consultant is competent? Does the laboratory have a policy/procedure to determine consultant competency? Use D6030 or D6103.

How does the laboratory evaluate personnel for consistency in slide review, (e.g., ANA, manual differential, urine sediment)?

D5211

§493.1236 Standard: Evaluation of proficiency testing performance.

(a) The laboratory must review and evaluate the results obtained on proficiency testing performed as specified in subpart H of this part.

Probes §493.1236(a)

Is there evidence of review and evaluation of the laboratory's proficiency testing (PT) results?

§493.1236 Standard: Evaluation of proficiency testing performance.

(b) The laboratory must verify the accuracy of the following:

D5213

§493.1236 Standard: Evaluation of proficiency testing performance.

(b)(1) Any analyte or subspecialty without analytes listed in subpart I of this part that is not evaluated or scored by a CMS-approved proficiency testing program.

Interpretative Guideline §493.1236(b)(1)

An analyte may not be evaluated or scored by the PT program if there are less than 10 participants in a particular peer group.

D5215

§493.1236 Standard: Evaluation of proficiency testing performance.

(b)(2) Any analyte, specialty or subspecialty assigned a proficiency testing score that does not reflect laboratory test performance (that is, when the proficiency testing program does not obtain the agreement required for scoring as specified in subpart I of this part, or the laboratory receives a zero score for nonparticipation, or late return or results).

Interpretative Guidelines §493.1236(b)(2)

The laboratory must have a mechanism for routine review of its proficiency testing results that are evaluated by its PT providers. This includes a review of its actual PT results against the PT provider's participant summary results for the particular PT event and when any of the following occur:

- The PT program assigned an artificial score of 100% (e.g., results not evaluated or scored);
- A zero score for nonparticipation; if the laboratory did not test the specimen, it must document what other means were used to assess the accuracy of the test for the PT event that was missed; or
- The PT provider notifies the laboratory that its results were not evaluated (given a score of "0") due to missing the return deadline.

Probes §493.1236(b)(2)

Has the laboratory reviewed its test menu to determine if it tests any analyte(s) that are not listed in subpart I?

§493.1236 Standard: Evaluation of proficiency testing performance.

(c) At least twice annually, the laboratory must verify the accuracy of the following:

D5217

§493.1236 Standard: Evaluation of proficiency testing performance.

(c)(1) Any test or procedure it performs that is not included in subpart I of this part.

Interpretative Guidelines §493.1236(c)(1)

Refer to subpart I, *Proficiency Testing Programs for Nonwaived Testing*. Subpart I includes those specialties, subspecialties, and analytes that are considered regulated tests. For those tests not listed in subpart I (not regulated), the laboratory must verify the accuracy of the test or procedure twice annually.

D5219

§493.1236 Standard: Evaluation of proficiency testing performance.

(c)(2) Any test or procedure listed in subpart I of this part for which compatible proficiency testing samples are not offered by a CMS-approved proficiency testing program.

Interpretative Guidelines §493.1236(c)(2)

Laboratory tests or procedures that are not compatible may include new or emerging technologies for which PT is not yet available.

Probes §493.1236(c)(2)

How does the laboratory verify accuracy of tests not included under subpart I or tests for which compatible PT samples are not available (e.g., blind testing of materials with known values, other external assessment programs, split samples with another laboratory instrument or method, comparison with Kodachrome slides from a reference source)?

D5221

§493.1236 Standard: Evaluation of proficiency testing performance.

(d) All proficiency testing evaluation and verification activities must be documented.

Interpretative Guidelines §493.1236(d)

Documentation must include review of all unsatisfactory scores and the corrective action taken.

D5291

§493.1239 Standard: General laboratory systems quality assessment.

(a) The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess, and, when indicated, correct problems identified in the general laboratory systems requirements specified at §§493.1231 through 493.1236.

Interpretative Guidelines §493.1239(a)-(c)

Quality Assessment (QA) is an ongoing review process that encompasses all facets of the laboratory's technical and non-technical functions and all locations/sites where testing is performed. QA also extends to the laboratory's interactions with responsibilities to patients, physicians, and other laboratories ordering tests, and the other non-laboratory areas or departments of the facility of which it is a part.

When the laboratory discovers an error or identifies a potential problem, actions must be taken to correct the situation. This correction process involves identification and resolution of the problem, and development of policies that will prevent recurrence. Policies for preventing problems that have been identified must be written as well as communicated to the laboratory personnel and other staff, clients, etc., as appropriate. Over time, the laboratory must monitor the corrective action(s) to ensure the action(s) taken have prevented recurrence of the original problem.

All pertinent laboratory staff must be involved in the assessment process through discussions or active participation.

QA of the General Laboratory System includes assessing practices/issues related to:

- *Patient confidentiality;*
- *Specimen identification and integrity;*
- *Complaint investigations;*
- *Communications;*
- *Personnel competency; and*
- *Proficiency testing performance.*

An example would be monitoring the type and number of complaints received by the laboratory such as a particular client continuously complaining about the laboratory's failure to promptly respond to STAT test requests. The laboratory must have documentation that the complaint was investigated and appropriate action taken to correct the problem.

Verify that the laboratory has a system in place for monitoring and evaluating confidentiality of patient information.

Probes §493.1239(a)

How does the laboratory assure that an individual who had problems in performance is competent after appropriate retraining and technical assistance is completed?

How does the laboratory determine which complaints require investigation and which do not?

D5293

§493.1239 Standard: General laboratory systems quality assessment.

(b) The general laboratory systems quality assessment must include a review of the effectiveness of corrective actions taken to resolve problems, revision of policies and procedures necessary to prevent recurrence of problems, and discussion of general laboratory systems quality assessment reviews with appropriate staff.

Interpretative Guidelines §493.1239(b)

Review assessment policies, procedures and reports to verify that the laboratory has a system in place to ensure continuous improvement. Corrective action reports are one indication that the laboratory is monitoring and evaluating laboratory performance and the quality of services.

Probes §493.1239(b)

When problems are identified in personnel competency, what corrective actions are instituted to assist employees to improve performance?

When the laboratory identifies a problem, are corrective actions taken, the resolution documented and monitored for effectiveness?

How does the laboratory prevent reoccurrences of problems?

How does the laboratory document and identify potential communication problems and corrective actions taken (e.g., with staff, referral laboratories)?

Have the corrective actions taken as a result of failures in proficiency testing (PT) and/or verification of accuracy testing as required under subpart H, improved performance?

(c) The laboratory must document all general laboratory systems quality assessment activities.

Interpretative Guidelines §493.1239(c)

The steps taken by the laboratory to identify and correct problems, and prevent their recurrences must be documented. All laboratory policies amended due to its QA activities must be noted.

D5300

Preanalytic Systems

§493.1240 Condition: Preanalytic systems.

Each laboratory that performs nonwaived testing must meet the applicable preanalytic system(s) requirements in §§493.1241 and 493.1242, unless HHS approves a procedure, specified in Appendix C of the State Operations Manual #7, that provides equivalent quality testing. The laboratory must monitor and evaluate the overall quality of the preanalytic systems and correct identified problems as specified in §493.1249 for each specialty and subspecialty of testing performed.

Interpretive Guidelines §493.1240

Preanalytic refers to all steps taken prior to the actual testing of a patient specimen from the test request to the actual testing of the specimen. The preanalytic systems requirements include three distinct sections: test requests; specimen submission, handling, and referral; and preanalytic systems quality assessment.

Significant deficiencies cited under this condition may indicate deficiencies under personnel responsibilities. Use D5300 when deficiencies are identified that have the potential to, or adversely affect patient testing, are systemic and pervasive throughout the laboratory, and are not limited to any one specialty or subspecialty.

To determine which tests are categorized as waived or nonwaived testing (i.e., moderate and high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/cli/index.html]. Test systems, assays and examinations not included in this listing (i.e., not yet categorized) are considered high complexity.

D5301

§493.1241 Standard: Test request.

(a) The laboratory must have a written or electronic request for patient testing from an authorized person.

Interpretive Guidelines §493.1241(a)

An "authorized person" means an individual authorized under State law to order tests or receive test results, or both. If the State law does not address who may order tests and receive test results, then anyone may order tests and receive test results. However, the laboratory must follow the requirements in the Social Security Act regarding test ordering for reimbursement under Medicare.

To assure only the authorized person is ordering the test, a laboratory using electronic test requests may issue passwords.

Use of standing orders should be clearly defined in written policy, describing which tests may be covered by standing orders and at what interval standing orders should be reconfirmed.

D5303

§493.1241 Standard: Test request.

(b) The laboratory may accept oral requests for laboratory tests if it solicits a written or electronic authorization within 30 days of the oral request and maintains the authorization or documentation of its efforts to obtain the authorization.

Interpretive Guidelines §493.1241(b)

Review the laboratory's policy for requesting written orders within 30 days of the oral requests. If no written order was received, verify the laboratory has documentation showing the attempt.

D5305

§493.1241 Standard: Test request.

(c) The laboratory must ensure the test requisition solicits the following information:

(c)(1) The name and address or other suitable identifiers of the authorized person requesting the test and, if appropriate, the individual responsible for using the test results, or the name and address of the laboratory submitting the specimen, including, as applicable, a contact person to enable the reporting of imminently life threatening laboratory results or panic or alert values.

Interpretive Guidelines §493.1241(c)(1)-(c)(8)

The address of the individual or laboratory requesting a test and/or using the test results should include the street, city or town and State of the individual or laboratory ordering or responsible for utilizing the test result. When appropriate, a telephone number or other mechanism to contact the individual responsible for using the test results should be provided to the laboratory.

If any information is missing from the test requisition or patient medical record or chart, the laboratory must determine whether to test the specimen. Laboratories must either obtain the missing information or report results and indicate on the test report, medical record or chart any limitations of test results due to the omission of patient information. If the missing information is essential (such as the family history for certain genetic tests) for accurate test results, it must be obtained prior to reporting patient test results.

Verify that test requisitions solicit all information necessary for the proper interpretation of results. This may include patient's age, sex, date and time of collection, specimen type (e.g., plasma, urine, spinal fluid), diagnosis, and date of last menstrual period (LMP) for Papanicolaou (PAP) smears. Verify that the instructions to clients are clear and specify the items that must be completed.

(c)(2) The patient's name or unique patient identifier.

(c)(3) The sex and age or date of birth of the patient.

(c)(4) The test(s) to be performed.

(c)(5) The source of the specimen, when appropriate.

(c)(6) The date and, if appropriate, time of specimen collection.

(c)(7) For Pap smears, the patient's last menstrual period, and indication of whether the patient had a previous abnormal report, treatment, or biopsy.

(c)(8) Any additional information relevant and necessary for a specific test to ensure accurate and timely testing and reporting of results, including interpretation, if applicable.

Interpretive Guidelines §493.1241(c)(8)

This may include such items as preventative or therapeutic medications, or family history.

Probes §493.1241(c)(1)-(c)(8)

How does the laboratory uniquely identify patient specimens that share the same or similar name, birth date, address or sex?

How does the requisition provide for inclusion of additional information when necessary (e.g., specimen type or source)?

D5307

§493.1241 Standard: Test request.

(d) The patient's chart or medical record may be used as the test requisition or authorization but must be available to the laboratory at the time of testing and available to

CMS or a CMS agent upon request.

Probes §493.1241(d)

When the patient's chart or medical record is used as the test requisition does it provide all the information necessary to ensure accurate testing and reporting of results?

D5309

§493.1241 Standard: Test request.

(e) If the laboratory transcribes or enters test requisition or authorization information into a record system or a laboratory information system, the laboratory must ensure the information is transcribed or entered accurately.

Interpretive Guidelines §493.1241(e)

The laboratory must have an ongoing mechanism to ensure the accuracy of manual entries by personnel into an LIS.

How does the laboratory ensure that all individuals who enter data including clerical staff correctly match patient information?

D5311

§493.1242 Standard: Specimen submission, handling, and referral.

(a) The laboratory must establish and follow written policies and procedures for each of the following, if applicable:

(a)(1) Patient preparation.

Probes §493.1242(a)(1)

How does the laboratory ensure that all staff including phlebotomists gives appropriate instructions for patient preparation when needed?

Does the laboratory provide instructions directly to patients or to the client when proper patient preparation is required for optimal specimen collection? For example:

- *Proper preservation (temperature) and transportation time of semen specimens;*
- *Fasting instructions for lipid profile testing;*
- *Dietary restrictions prior to occult blood testing;*
- *Twenty-four hour urine collection for specific tests; and*
- *Fasting and two hour post-prandial glucose collections.*

If a patient has special communication (hearing impaired, not fluent in English, etc.) needs, are resources available to the client or to the patient, as appropriate, to ensure instructions for specimen collection, preservation, and transportation to the laboratory are properly understood?

Has the laboratory provided to its staff and/or individuals external to the laboratory who collect specimens, written procedures to ensure that patient preparation requirements have been followed?

(a)(2) Specimen collection.

Interpretive Guidelines §493.1242(a)(2)

Verify that procedures are available to the appropriate staff responsible for collecting the

correct specimen, that personnel are using the appropriate collection technique (order and site of draw) and proper containers (e.g., acceptable anti-coagulant, sterile containers for culture specimens, dacron swabs vs. cotton swabs).

(a)(3) Specimen labeling, including patient name or unique patient identifier and, when appropriate, specimen source.

Interpretive Guidelines §493.1242(a)(3)

If the laboratory receives two specimens simultaneously with the same first and last name or birth date, the laboratory must have a system in place to process these specimens using distinct identifying indicators in order to distinguish between the specimens. This also pertains to personnel collecting and labeling specimens. This may include a system that involves labeling the specimen container and request slip (or the patient's medical record or chart) with a unique patient identification number, but does not preclude the use of other mechanisms to assist in patient identification and tracking of specimens throughout the collection, accessioning, testing, and reporting processes.

(a)(4) Specimen storage and preservation.

Interpretive Guidelines §493.1242(a)(4)

Review manufacturer's instructions for performance of each test method to ensure that specimens are properly stored (e.g., maintained at room temperature, kept refrigerated after separation, separated and frozen).

Probes §493.1242(a)(4)

What instructions are provided for specimen preservation and transportation, when applicable? For example:

- *Sputum for Cytology;*
- *Specimens for parathyroid hormone;*
- *Specimens for blood gas analysis;*
- *Specimens for urine culture and colony count; and*
- *Specimens for 24 hour urine collections requiring preservatives.*

(a)(5) Conditions for specimen transportation.

Probes §493.1242(a)(5)

Does the laboratory follow the manufacturer's or the referral laboratory's instructions, as appropriate, for transport of specimens?

(a)(6) Specimen processing.

Interpretive Guidelines §493.1242(a)(6)

Specimen processing may include receiving the specimen, accessioning the specimen, preparing the specimen for in-house analysis, preparation to send to a reference laboratory, preparing slides, and inoculating primary culture media, etc. Specimen processing also includes for: Parasitology: the fixation and concentration of specimens; Virology: the pretreatment of specimens with antibiotics, the manipulation of cell culture tubes and inoculation of the cell cultures prior to incubation; Mycobacteriology: performing digestion-decontamination and concentration procedures on clinical specimens; and Histopathology: fixation, embedding, cutting, mounting, staining and coverslipping.

Probes §493.1242(a)(6)

What policies or systems does the laboratory have in place to differentiate specimens that have similar names or identification information?

How does the laboratory recognize and process timed patient specimens (e.g., peaks, and troughs)?

(a)(7) Specimen acceptability and rejection.

Interpretive Guidelines §493.1242(a)(7)

Criteria for specimen acceptability and rejection must include the disposition of the rejected specimen(s). Use D5805. The laboratory should promptly notify the authorized person when a specimen meets its rejection criteria and is unsuitable for testing.

(a)(8) Specimen referral.

Interpretive Guidelines §493.1242(a)(8)

Ensure that the laboratory has a current service manual available for each reference laboratory that it uses that contains the reference laboratory's specimen requirements for the test to be performed.

Probes §493.1242(a)(8)

Are laboratory personnel familiar with procedures to prepare and/or submit specimens to the appropriate reference laboratory?

How does the laboratory ensure the security and preservation of specimens submitted to their reference laboratory (e.g., if the office closes before the arrival of the reference laboratory's courier)? How does the laboratory ensure a timely pick-up of specimens to be performed at the referral laboratory?

D5313

§493.1242 Standard: Specimen submission, handling, and referral.

(b) The laboratory must document the date and time it receives a specimen.

Interpretive Guidelines §493.1242(b)

When a sample is collected and a test is performed during the course of a patient's visit, the date and time recorded in the patient "sign-in" log may be used as the date and time of receipt into the laboratory.

D5315

§493.1242 Standard: Specimen submission, handling, and referral.

(c) The laboratory must refer a specimen for testing only to a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by CMS.

Interpretive Guidelines §493.1242(c)

Some examples of laboratories meeting equivalent requirements are those of the Veterans Administration (VA), the Department of Defense (DOD) facilities, and CLIA-exempt laboratories.

Probes §493.1242(c)

How does the laboratory ensure that the reference laboratory has and maintains a current CLIA certificate?

D5317

§493.1242 Standard: Specimen submission, handling, and referral.

(d) If the laboratory accepts a referral specimen, written instructions must be available to the laboratory's clients and must include, as appropriate, the information specified in paragraphs (a)(1) through (a)(7) of this section.

Interpretive Guidelines §493.1242(d)

Ensure the laboratory has provided written instructions to each client that sends specimens/test requests. The instructions may contain information on specimen handling (e.g., collection, preservation, storage, transport, testing schedule times and how to obtain additional assistance for unusual circumstances).

D5391

§493.1249 Standard: Preanalytic systems quality assessment.

(a) The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess, and when indicated, correct problems identified in the preanalytic systems specified at §§493.1241 through 493.1242.

Interpretive Guidelines §493.1249(a)-(c)

Quality Assessment (QA) is an ongoing review process that encompasses all facets of the laboratory's technical and non-technical functions and all locations/sites where testing is performed. QA also extends to the laboratory's interactions with and responsibilities to patients, physicians, and other laboratories ordering tests, and the other non-laboratory areas or departments of the facility of which it is a part.

When the laboratory discovers an error or identifies a potential problem, actions must be taken to correct the situation. This correction process involves identification and resolution of the problem, and development of policies that will prevent recurrence. Policies for preventing problems that have been identified must be written as well as communicated to the laboratory personnel and other staff, clients, etc., as appropriate. Over time, the laboratory must monitor the corrective action(s) to ensure the action(s) taken have prevented recurrence of the original problem. All pertinent laboratory staff must be involved in the assessment process through discussions or active participation.

*QA of the **Preanalytic System** includes assessing practices/issues related to test requests, specimen submission, handling and referral.*

Some examples include: monitoring the frequency of specimen handling problems (such as the use of an improper blood collection tube, inadequate mixing of blood specimens with anticoagulant after collection), and delays in specimen transport; identifying clients who repeatedly refer unacceptable specimens or improperly complete requisition forms and documentation of its efforts to reduce the recurrence of these problems.

Review assessment policies, procedures and reports to verify that the laboratory has a system in place to ensure continuous improvement. Corrective action reports are one indication that the laboratory is monitoring and evaluating laboratory performance and the quality of services.

Probes §493.1249(a)-(c)

When a laboratory uses off-site drawing facilities, what policies or procedures does the

laboratory use to ensure proper accountability or tracking of patient specimens from time of collection to receipt by the laboratory performing the tests?

Does the laboratory perform periodic or spot checks for accurate transfer of information

(e.g., manual entries by personnel from test orders to test requisition or into an LIS)? For referral specimens, how does the laboratory check for transcription errors when patient test information is transcribed from the laboratory's original requisition form to the reference laboratory's requisition?

What actions does the laboratory take if test requisitions from one or more clients are consistently incomplete, illegible or contain incorrect information?

What actions does the laboratory take if specimens received from one client are consistently unsatisfactory for testing (e.g., specimens for Cytology)? Has the laboratory's efforts to reduce the recurrence of these problems been documented and effective?

D5393

§493.1249 Standard: Preanalytic systems quality assessment.

(b) The preanalytic systems assessment must include a review of the effectiveness of corrective actions taken to resolve problems, revision of policies and procedures necessary to prevent recurrence of problems, and discussion of preanalytic systems quality assessment reviews with appropriate staff.

(c) The laboratory must document all preanalytic systems quality assessment activities.

Interpretative Guidelines §493.1249(c)

The steps taken by the laboratory to identify and correct problems and prevent their recurrence must be documented. All laboratory policies amended due to its QA activities must also be noted.

D5400

Analytic Systems

§493.1250 Condition: Analytic Systems.

Each laboratory that performs nonwaived testing must meet the applicable analytic systems requirements in §§493.1251 through 493.1283, unless HHS approves a procedure, specified in Appendix C of the State Operations Manual #7, that provides equivalent quality testing. The laboratory must monitor and evaluate the overall quality of the analytic systems and correct identified problems as specified in §493.1289 for each specialty and subspecialty of testing performed.

NOTE: *Throughout the analytic systems section, the regulations require laboratories to follow test system manufacturer's instruction for performing the testing. This means the laboratory must perform and follow the manufacturer's package insert as approved or cleared by the FDA.*

Interpretive Guidelines §493.1250

Significant deficiencies cited under this condition may indicate deficiencies under

personnel. Use D5400 when deficiencies are identified that are significant and have the potential to, or adversely affect patient testing, are systemic and pervasive throughout the laboratory, and are not limited to any one specialty or subspecialty.

Refer to §§493.1261 - 493.1278 for additional requirements for Bacteriology, Mycobacteriology, Mycology, Parasitology, Virology, Routine Chemistry, Hematology, Immunohematology, Histopathology, Cytology, Clinical Cytogenetics, and Histocompatibility.

D5401

§493.1251 Standard: Procedure Manual.

(a) A written procedures manual for all tests, assays, and examinations performed by the laboratory must be available to, and followed by, laboratory personnel. Textbooks may supplement but not replace the laboratory's written procedures for testing or examining specimens.

Interpretive Guidelines §493.1251(a)

Procedures may be organized in the form of manuals, stored in computers and/or card files. Use D5403, if the procedure manual lacks any of the applicable information as specified in §493.1251(b)(1)-(14). If the laboratory has procedures that are not used for test performance, but are used for reference purposes, they may be placed in a reference section. You need not review reference procedures unless problems are identified with patient test results.

Centers for Disease Control and Prevention (CDC) and Armed Forces Institute of Pathology (AFIP) manuals, manufacturer's operating instructions, and package inserts, are acceptable provided the policies and procedures are available, and the methods in use are clearly indicated. If the laboratory modifies any procedure, the modification must be documented and verified/established as specified in §493.1253.

Probes §493.1251(a)

How does the laboratory ensure that personnel follow the procedures in the procedure manual? How are changes in procedures communicated to laboratory personnel? For competency issues, use D6030 or D6103 as applicable.

D5403

§493.1251 Standard: Procedure Manual.

(b) The procedure manual must include the following when applicable to the test procedure:

(b)(1) Requirements for patient preparation; specimen collection, labeling, storage, preservation, transportation, processing, and referral; and criteria for specimen acceptability and rejection as described in §493.1242.

Interpretive Guidelines §493.1251(b)(1)

If testing is delayed or not performed daily, specimens must be preserved or stored in accordance with the laboratory's procedures to assure specimen integrity.

Determine if the laboratory has a procedure for handling and identifying aliquotted specimens; e.g., sputum sent for Mycobacteriology and Cytology examinations; stool specimens for occult blood, routine culture, parasitology and C.difficile toxin assay; and

cerebrospinal fluids for cell count, culture, glucose and protein.

(b)(2) Microscopic examination, including the detection of inadequately prepared slides.

(b)(3) Step-by-step performance of the procedure, including test calculations and interpretation of results.

(b)(4) Preparation of slides, solutions, calibrators, controls, reagents, stains, and other materials used in testing.

(b)(5) Calibration and calibration verification procedures.

Interpretive Guidelines §493.1251(b)(5)

Calibration and calibration verification procedures must be established in accordance with §493.1255.

(b)(6) The reportable range for test results for the test system as established or verified in §493.1253.

(b)(7) Control procedures.

Interpretive Guidelines §493.1251(b)(7)

Determine if the laboratory's quality control procedures include the following:

- *Type of control (e.g., manufacturer or in-house, electronic);*
- *Identity (e.g., normal, abnormal, level I, II, patient or a control);*
- *Number and frequency of testing controls;*
- *Control limits established in accordance with §§493.1253 and 493.1256; and*
- *Criteria to determine acceptable control results.*

(b)(8) Corrective action to take when calibration or control results fail to meet the laboratory's criteria for acceptability.

Interpretive Guidelines §493.1251(b)(8)

Ensure that corrective action procedures are established in accordance with §493.1282(b)(2).

(b)(9) Limitations in the test methodology, including interfering substances.

(b)(10) Reference intervals (normal values).

(b)(11) Imminently life-threatening test results, or panic or alert values.

(b)(12) Pertinent literature references.

(b)(13) The laboratory's system for entering results in the patient record and reporting patient results including, when appropriate, the protocol for reporting imminent life threatening results, or panic, or alert values.

Interpretive Guidelines §493.1251(b)(13)

Ensure the procedure manual provides instructions for reporting the patient's test results in the appropriate units or terminology. Use D5805.

Probes §493.1251(b)(13)

Do laboratory procedures address the process for reporting (oral and written) results on patients with multiple laboratory encounters to ensure that the exact name, date, time and identification of specimen is conveyed to the authorized person?

(b)(14) Description of the course of action to take if a test system becomes inoperable.

Interpretive Guidelines §493.1251(b)(14)

Laboratory information systems (LIS) procedures must be available to operators. Instructions should identify the individual(s), either by name or position, to notify if the LIS goes down or if a system error occurs.

Probes §493.1251(b)(14)

When the primary testing system is inoperable, what procedure does the laboratory use to bring the backup system on line?

D5405

§493.1251 Standard: Procedure Manual.

c) Manufacturer's test system instructions or operator manuals may be used, when applicable, to meet the requirements of paragraphs (b)(1) through (b)(12) of this section. Any of the items under paragraphs (b)(1) through (b)(12) of this section not provided by the manufacturer must be provided by the laboratory.

D5407

§493.1251 Standard: Procedure Manual.

(d) Procedures and changes in procedures must be approved, signed, and dated by the current laboratory director before use.

Interpretive Guidelines §493.1251(d)

Verify that the methods in the procedure manual are current for tests offered by the laboratory (e.g., reagent test kits and instruments used in the laboratory correlate with methods in the procedure manual).

All laboratory procedures including CDC and AFIP manuals, manufacturer's operator manuals, and package inserts must reflect the director's review and approval including any modifications in the procedure.

Approval of procedures is the responsibility of the laboratory director. A coversheet may be used for the director to approve the manual. Annual review of procedures is not required.

D5409

§493.1251 Standard: Procedure Manual.

e) The laboratory must maintain a copy of each procedure with the dates of initial use and discontinuance as described in §493.1105(a)(2).

D5411

§493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies.

a) Test systems must be selected by the laboratory. The testing must be performed following the manufacturer's instructions and in a manner that provides test results within the laboratory's stated performance specifications for each test system as determined under §493.1253.

Interpretive Guidelines §493.1252(a)

Following manufacturer's instructions means that the laboratory complies with the recommendations, suggestions and requirements in package inserts and/or instrument operator manuals. These include, but are not limited to:

- Handling reagents, materials, and supplies;
- Adhering to conditions for storage and testing; and
- Performing equipment maintenance and function checks.

For Immunology tests such as Syphilis Serology, check for the following parameters:

- Antigen volume;
- Incubation time and temperature;
- Light source;
- Rotator speed and circumference; and
- Conjugate titer.

Probes §493.1252(a):

Are instruments with adjustable settings appropriately set for each substance or cell to be analyzed (e.g., gamma counters, flow cytometry)?

D5413

§493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies.

(b) The laboratory must define criteria for those conditions that are essential for proper storage of reagents and specimens, accurate and reliable test system operation, and test result reporting. The criteria must be consistent with the manufacturer's instructions, if provided. These conditions must be monitored and documented and, if applicable, include the following:

(b)(1) Water quality.

(b)(2) Temperature.

(b)(3) Humidity.

(b)(4) Protection of equipment and instruments from fluctuations and interruptions in electrical current that adversely affect patient test results and test reports.

Interpretive Guidelines §493.1252(b)

Water quality is classified by several different organizations, such as NCCLS, into different reagent grades dependent on microbial content, resistivity, silicate content, and particulate matter. Each laboratory is expected to use the appropriate water quality as required for each instrument, kit, or test system. Laboratories producing water should consider parameters such as pH, silicate content, particulate matter, and bacterial and organic content in assessing water quality. These parameters vary by test system and should be assessed by the laboratory for appropriateness and monitoring. Laboratories purchasing water that has already been classified are not expected to evaluate the above parameters unless specified by the manufacturer or by the laboratory in its procedure manual.

Temperature-controlled spaces, equipment, and instruments must be monitored and results documented for acceptable temperature ranges. Corrective action is needed when acceptable temperature ranges are exceeded. Use D5757.

Continuous monitoring of temperatures by a recording thermograph is acceptable provided the data and time of use are annotated. The charts must be retained to document that temperatures were within the limits established by the laboratory.

In lieu of manual temperature recording, it is acceptable for temperatures to be maintained and monitored internally by the instrument, provided either test results are flagged or not generated when the temperature range for test performance is exceeded.

Probes §493.1252(b)(1)-(b)(4)

How does the laboratory provide special conditions when required for specimen or reagent storage?

How is room temperature and humidity monitored when necessary for test performance, proper operation of reagents, instruments, equipment, or laboratory computer systems?

When temperatures and/or humidity are outside acceptable limits, how does the laboratory rectify the problem?

How does the laboratory that moves from testing site to testing site demonstrate that the conditions necessary for quality testing are maintained?

When mobile laboratory or temporary testing site equipment is not in use (weekends, overnight) how are instruments, reagents, stains, and other solutions protected from extreme temperature fluctuations?

D5415

§493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies.

(c) Reagents, solutions, culture media, control materials, calibration materials, and other supplies, as appropriate, must be labeled to indicate the following:

(c)(1) Identity and when significant, titer, strength or concentration.

(c)(2) Storage requirements.

(c)(3) Preparation and expiration dates.

Interpretive Guidelines §493.1252(c)(3)

Expiration dates for test kits and/or reagents may differ due to date opened or storage conditions (e.g., refrigerator, room temperature). Verify that laboratory personnel are aware of these differences and document the appropriate expiration date.

(c)(4) Other pertinent information required for proper use.

D5417

§493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies.

(d) Reagents, solutions, culture media, control materials, calibration materials, and other supplies must not be used when they have exceeded their expiration date, have deteriorated, or are of substandard quality.

Interpretive Guidelines §493.1252(d)

In citing deficiencies, for outdated or deteriorated materials, indicate whether these materials have been used for patient testing. Also, look for contamination, drying or other signs of deterioration. This is as important as checking expiration dates.

The laboratory must comply with the Food and Drug Administration (FDA) product dating requirements of 21 CFR 610.53 for blood products and other biologicals, and labeling requirements, as cited in 21 CFR 809.10 for all other in vitro diagnostics. Any exception to the product dating requirements in 21 CFR 610.53 will be granted by the FDA in the form of an amendment of the product license, in accordance with

21 CFR 610.53(d). All exceptions must be documented by the laboratory.

D5419

§493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies.

(e) Components of reagent kits of different lot numbers must not be interchanged unless otherwise specified by the manufacturer.

Interpretive Guidelines §493.1252(e)

"Kit" means all components of a test that are packaged together.

§493.1253 Standard: Establishment and verification of performance specifications.

(a) Applicability. Laboratories are not required to verify or establish performance specifications for any test system used by the laboratory before April 24, 2003.

Interpretive Guidelines §493.1253(a)

The requirements of §493.1253 apply to each nonwaived test system (i.e., moderate and high complexity) introduced into the laboratory on or after April 24, 2003. This includes the following:

- *A test system that is introduced into the laboratory for the first time to measure an analyte that the laboratory has not previously measured;*
- *A test system introduced for the first time into the laboratory for a test that the laboratory currently performs on an alternative test system (e.g., instrument A has been used to perform cholesterol testing, now instrument B will be used);*
- *An analyte added to a test system that can measure multiple analytes which the laboratory has been using for patient testing but has not previously reported patient results for this particular analyte; and*
- *A modification to a test system that the laboratory has been using for patient testing (e.g., the laboratory reduces the specimen and/or reagent volumes).*

When multiple instruments (including the same make and model, e.g., point-of-care instruments) are used to perform the same test, the laboratory must verify or establish, as applicable, performance specifications for each instrument.

Refer to requirements in subpart M, for training and competency of personnel.

Prior to testing patient specimens, the laboratory should begin the process of establishing the assay or test system's performance specifications by performing the following:

- *Obtain and review test performance data from the test development source (e.g., Centers for Disease Control and Prevention), including number of tests performed on different patient groups or specimen types, preliminary data on sensitivity, specificity, and accuracy, precision, interfering substances, etc.*
- *Use testing personnel that have been trained and demonstrated competency performing the same methodology for other agents.*

As soon as control/calibration materials become available, the applicable requirements in §493.1253 must be met.

Specific information regarding testing for agents of emergent public health significance and alternative methods /procedures for establishing performance specifications may be found at www.cdc.gov.

NOTE: Public health testing performed on environmental (non-human) samples is not subject to CLIA.

D5421

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(1) Verification of performance specifications. Each laboratory that introduces an unmodified, FDA-cleared or approved test system must do the following before reporting patient test results:

Interpretive Guidelines §493.1253(b)(1)

The laboratory is responsible for verifying the performance specifications of each nonwaived unmodified FDA-cleared or approved test system that it introduces, prior to reporting patient test results. The verification of method performance should provide evidence that the accuracy, precision, and reportable range of the procedure are adequate to meet the clients' needs, as determined by the laboratory director and clinical consultant. A laboratory may use the manufacturer's performance specifications as a guideline, but is responsible for verifying the manufacturer's analytical claims before initiating patient testing.

*When a temporary replacement (loaner) instrument is received which is identical (i.e., same make and model, and method for the same analyte) to the instrument which is being replaced, the laboratory must verify comparable performance by comparing, at a minimum, results of two or more levels of controls **and** either previously tested proficiency samples or previously tested patient specimens.*

If a method was verified by someone other than the laboratory staff (e.g., manufacturer representative), the laboratory must demonstrate that this verification correlates with its in-house test performance. This may be accomplished by the laboratory testing "known" samples.

For some qualitative tests, the laboratory may verify the manufacturer's specifications by testing known positive and negative samples to assure that the expected results are obtained. (Specimens of known quantitative value may be used to verify the accuracy of a qualitative test.)

Prior to introducing a test for routine patient testing, the laboratory must review and evaluate the verification data.

Each laboratory is responsible for determining that its performance specifications for each test system are not affected by the relocation of the laboratory or test system. (See manufacturer's package insert regarding critical requirements such as set-up, limitations, environmental conditions, etc.)

If calibration material is used to verify method performance specifications, the laboratory must demonstrate that there is a minimal matrix effect and the calibration material is appropriate for verifying test system performance specifications.

If the LIS performs any calculations to determine a laboratory result, the calculations must be verified immediately after the LIS is programmed and prior to initial calculation of patient results.

"Less than" is used for reporting test results that are below the laboratory's detection limits for an analyte. (Detection limits must be established through method verification.) "Equivalent designation" is used to report test results for those methods that yield results below a clinically significant level (e.g., for a quantitative immunology test, patient results may be clinically negative at a 1:8 titer and test results may be reported as "1:8 negative). (The normal value is 1:8 or less.) "Greater than" is used for reporting test results that are above the laboratory's detection limits for an analyte. If patient test results exceed the laboratory's reportable range, the laboratory must report the result as greater than the highest detection limit, reassay a diluted patient specimen and report the calculated result, or send the specimen to a reference laboratory.

Probes §493.1253(b)(1)

How does the laboratory determine if a new or revised LIS program (whether purchased or developed in-house) performs acceptably before it is integrated into routine operation?

(b)(1)(i) Demonstrate that it can obtain performance specifications comparable to those established by the manufacturer for the following performance characteristics:

Interpretive Guidelines §493.1253(b)(1)(i)

Laboratories may simultaneously verify multiple performance specifications by choosing appropriate samples; e.g., repeatedly test (precision) samples with known (accuracy) high and low values (reportable range). This testing should be performed among all operators on different days. In addition, for test systems of the same make and model, consider verifying performance specifications of these devices at the same time.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(1)(i)(A) Accuracy.

Interpretive Guidelines §493.1253(b)(1)(i)(A)

Accuracy- The laboratory is responsible for verifying that the method produces correct results. Verification of accuracy, may be accomplished by:

- Testing reference materials;
- Comparing results of tests performed by the laboratory against the results of a reference method; or
- Comparing split sample results with results obtained from a method, which is shown to provide clinically valid results.

For qualitative methods, the laboratory must verify that a method will identify the presence/absence of the analyte.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(1)(i)(B) Precision.

Interpretive Guidelines §493.1253(b)(1)(i)(B)

Precision (Reproducibility)- The laboratory is responsible for verifying the precision of each test system by assessing day-to-day, run-to-run, and within-run variation, as well as operator variance. This may be accomplished by:

- Repeat testing of known patient samples over time;
- Testing QC material in duplicate and over time; or
- Repeat testing of calibration materials over time.

EXCEPTION: For fully automated systems that are not user dependent, operator variance does not need to be evaluated.

(b)(1)(i)(C) Reportable range of test results for the test system.

Interpretive Guidelines §493.1253(b)(1)(i)(C)

Reportable Range- The laboratory is responsible for verifying the reportable range of patient test results for each test system. Verification of reportable range, may be accomplished by:

- *Assaying low and high calibration materials or control materials; or*
- *Evaluating known samples of abnormal high and abnormal low values.*

Hematology whole blood high range calibration materials are not generally available. Therefore, laboratories may use patient specimens with verified elevated cell counts to verify the upper limit of the reportable range.

Probes §493.1253(b)(1)(i)(c)

If a dilution procedure is used when patient results exceed the test system's reportable range, how does the laboratory assure the appropriate diluent is used for each type of specimen?

How does the laboratory verify and document the accuracy of the results for diluted specimens?

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(1)(ii) Verify that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population.

Interpretive Guidelines §493.1253(b)(1)(ii)

Reference Range (Normal Values) - The laboratory may use the manufacturer's reference range provided it is appropriate for the laboratory's patient population (i.e., a normal range that reflects the type of specimen and demographic variables such as age and sex, as applicable). If the manufacturer has not provided reference ranges appropriate for the laboratory's patient population, the laboratory may use published reference range(s). The laboratory must evaluate an appropriate number of specimens to verify the manufacturer's claims for normal values or, as applicable, the published reference ranges.

D5423

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2) Establishment of performance specifications. Each laboratory that modifies an FDA-cleared or approved test system, or introduces a test system not subject to FDA clearance or approval (including methods developed in-house and standardized methods such as text book procedures, or uses a test system in which performance specifications are not provided by the manufacturer must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics, as applicable:

Interpretive Guidelines §493.1253(b)(2)

Prior to reporting patient test results, the laboratory is responsible for establishing the performance specifications for each modified FDA-cleared or approved test system, each test system not subject to FDA clearance or approval, and each test system for which the

manufacturer does not provide performance specifications. The establishment of method performance specifications should provide evidence that the accuracy, precision, analytical sensitivity, and analytical specificity of the procedure is adequate to meet the clients' needs as determined by the laboratory director and clinical consultant.

"Modified by the laboratory," means any change to the assay that could affect its performance specifications for sensitivity, specificity, accuracy, or precision, etc. Laboratory modification of the manufacturer's instructions that could affect performance specification's include but are not limited to:

- Change in specimen handling instructions;
- Incubation times or temperatures;
- Change in specimen or reagent dilution;
- Using a different calibration material (or changing the manufacturer's set-points);
- Introducing a different antibody (source, monoclonal-vs-polyclonal);
- Change or elimination of a procedural step;
- Change or addition of detector (conjugate) or substrate;
- Change in the solid phase;
- Change in the cutoff or method of calculating the cutoff for semi-quantitative assays;
- Change in the endpoint or calculation of the endpoint;
- Addition of adsorbent;
- Change in the strain of antigen in serologic assays; and
- Changing the calibrator/reference material.

EXCEPTIONS: Use of reagents that are exempt from the premarket notification procedures in 21 CFR 807 for an instrument produced by another manufacturer is not considered a method modification. If the FDA has cleared a manufacturer's reagents and/or calibration materials for use with an instrument produced by another manufacturer, the use of these reagents/materials is not considered a method modification and does not require establishment of performance specifications. However, the laboratory must verify performance specifications as required under §493.1253(b)(1). Verification of performance specifications is required if reagents are changed to those of another manufacturer.

"Modified by the laboratory," also means any change in intended use that could affect test system performance specifications for sensitivity, specificity, accuracy, and precision, etc., and the clinical utility of the test system. Changes in intended use are considered "off-label" use of a commercial test system. **CAUTION:** "Off-label" use is not supported by the manufacturer's clinical data and when identified, must be reported to the FDA.

Examples of changes in intended use are:

- Using a different sample matrix (plasma vs. urine);
- Using or promoting the test for another purpose (screening vs. diagnostic); and
- Changing the type of analysis (qualitative results reported as quantitative).

NOTE: Because analyte specific reagents (ASR) are not approved by the FDA, the laboratory is responsible for establishing performance specifications for the test systems using these reagents.

For automated or semi-automated analyzers, reprocessed (reconditioned) rotors/cuvettes which have passed quality control inspection criteria of the reprocessing company, and returned to the same laboratory that sent them for cleaning and re-use, is not considered a method modification.

Specimens of known quantitative value may be used to determine the laboratory's performance specifications for a qualitative test.

Each laboratory is responsible for determining that its performance specifications for each test method are not affected by the relocation of the laboratory or test system. (See manufacturer's package insert regarding critical requirements such as set-up, limitations, environmental conditions, etc.)

If calibration material is used to establish method performance specifications, the laboratory must demonstrate that there is a minimal matrix effect and the calibration material is appropriate for establishing test system performance specifications.

If the LIS performs any calculations to determine a laboratory result, the calculations must be verified immediately after the LIS is programmed and prior to initial calculation of patient results.

CMS policies for the establishment of performance specifications for new test assays or test systems used to detect agents of emergent public health significance will be forthcoming in future publications.

NOTE: *Public health testing performed on environmental (non-human) samples is not subject to CLIA.*

Probes §493.1253(b)(2)

How does the laboratory determine if a new or revised LIS program (whether purchased or developed in-house) performs acceptably before it is integrated into routine operation?

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(i) Accuracy.

Interpretive Guidelines §493.1253(b)(2)(i)

Accuracy-

The laboratory is responsible for establishing that the method produces correct results.

Establishment of accuracy, may be accomplished by:

- *Testing reference materials or comparing results of tests performed using an established reference method; or*
- *Comparing split sample results with results obtained from a method, which is shown to provide clinically valid results.*

For qualitative methods, the laboratory is responsible for establishing that a method will identify the presence/absence of the analyte.

In establishing a test system for a new analyte, research results may be used to document the accuracy of the test by correlation with the clinical presentation. In addition, the laboratory needs to determine the test system's precision and have mechanisms for determining analytical specificity, analytical sensitivity, and interfering substances.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(ii) Precision.

Interpretive Guidelines §493.1253 (b)(2)(ii)

Precision (Reproducibility)- *The laboratory is responsible for establishing the*

precision of each test system by assessing day-to-day, run-to-run, and within-run variation, as well as operator variance.

This may be accomplished by:

- Repeat testing of known patient samples over time;
- Testing QC material in duplicate and over time; or
- Repeat testing of calibration materials over time.

EXCEPTION: For fully automated systems that are not user dependent, operator variance does not need to be evaluated.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(iii) Analytical sensitivity.

Interpretive Guidelines §493.1253(b)(2)(iii)

Analytical Sensitivity- The laboratory is responsible for determining the lowest concentration or amount of the analyte or substance that can be measured or distinguished from a blank, i.e., minimum detection limits or how much of the analyte must be present to be measured.

For modified test systems, the laboratory may use the lower limit of the manufacturer's reportable range if it has demonstrated that the modification has not affected the lower limit.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(iv) Analytical specificity to include interfering substances.

Interpretive Guidelines §493.1253(b)(2)(iv)

Analytical Specificity - The laboratory must determine the extent to which the method measures the analyte for which it is reporting results.

Interfering Substances- The laboratory must document information regarding interfering substances from product information, literature, or its own testing. These may include: specimen hemolysis, anticoagulant, lipemia, and turbidity; patients' clinical conditions, disease states, and medications.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(v) Reportable range of test results for the test system.

Interpretive Guidelines §493.1253(b)(2)(v)

Reportable Range- The laboratory is responsible for establishing the upper and lower limits of the test system.

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(vi) Reference intervals (normal values).

Interpretive Guidelines §493.1253(b)(2)(vi)

Reference Range (Normal Values) - The laboratory must establish a reference range that is appropriate for the laboratory's patient population (i.e., a normal range that reflects the type of specimen and demographic variables such as age and sex, as applicable).

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(2)(vii) Any other performance characteristic required for test performance.

D5425

§493.1253 Standard: Establishment and verification of performance specifications.

(b)(3) *Determination of calibration and control procedures.* The laboratory must determine the test system's calibration procedures and control procedures based upon the performance specifications verified or established under paragraph (b)(1) or (b)(2) of this section.

Interpretive Guidelines §493.1253(b)(3)

Through the verification/establishment process, the laboratory defines the frequency for calibration and control performance as well as the type, number, and concentration of calibration and control materials used to monitor, detect error, and evaluate method performance. The frequency for calibration and control performance must not be less than the frequency specified in the manufacturer's instructions.

In establishing the calibration and quality control frequency, the laboratory must consider:

- *Test system instrument/reagent stability, including relocation;*
- *Frequency with which the test is performed;*
- *Technique dependence of the method;*
- *Frequency of quality control failures; and*
- *Training, experience, and competency of technical personnel.*

For additional criteria in determining calibration and quality control frequency refer to §§493.1255 and 493.1256.

§493.1253 Standard: Establishment and verification of performance specifications.

(c) *Documentation.* The laboratory must document all activities specified in this section.

Interpretive Guidelines §493.1253(c)

The actual measurement(s) taken, reactions and/or observations must be recorded. Acceptable formats for documentation may vary.

§493.1254 Standard: Maintenance and function checks.

(a) *Unmodified manufacturer's equipment, instruments, or test systems.* The laboratory must perform and document the following:

Interpretative Guideline §493.1254(a)

When a laboratory introduces a new test system, the laboratory may determine, depending on the outcome of the performance specifications, that additional measures are necessary in order to ensure accurate and reliable test results.

D5429

§493.1254 Standard: Maintenance and function checks.

(a)(1) Maintenance as defined by the manufacturer and with at least the frequency specified by the manufacturer.

Interpretive Guidelines §493.1254(a)(1)

"As defined by the manufacturer " means that the laboratory complies with the maintenance recommended in package inserts and/or instrument operator manuals for each piece of equipment/instrument it uses, including those that are peripherally involved in patient testing (e.g., incubators, centrifuges, safety cabinets, autoclaves and microscopes).

A laboratory's maintenance program is usually divided into two parts:

- *Unscheduled repairs when needed; and*
- *Scheduled preventive maintenance (PM), which is performed to prevent breakdowns or malfunctions, to prolong the life of an instrument and to maintain optimum operating characteristics.*

A service contract for PM from an outside source is acceptable provided that for each instrument or piece of equipment, there is a description of the service to be performed and frequency of service.

A service contract does not negate the laboratory's responsibility for performing other routine maintenance not included in the maintenance contract. Acceptable performance parameters (if applicable) must be documented.

The laboratory must perform and document maintenance as specified by the manufacturer for the LIS computer and devices such as monitors, printers and modems. All devices must be maintained to assure accurate, clear, and interference-free transmission.

Probes §493.1254(a)(1)

Are LIS system components (e.g., server, hard drives, disk packs) maintained according to the manufacturer's instructions?

When downtime is required to perform maintenance on LIS equipment, how are LIS users notified?

How does the laboratory's maintenance program assure that instruments and equipment maintain optimum operating characteristics and minimize breakdowns?

D5431

§493.1254 Standard: Maintenance and function checks.

(a)(2) Function checks as defined by the manufacturer and with at least the frequency specified by the manufacturer. Function checks must be within the manufacturer's established limits before patient testing is conducted.

Interpretive Guidelines §493.1254(a)(2)

Function checks refer to those activities performed to evaluate critical operating characteristics (e.g., stray light, zeroing, electrical levels, optical alignment, background counts, counting efficiency) according to the accepted method of operation for each type of device or instrument. Daily quality control activities and function checks are performed prior to patient testing to ensure that an instrument is functioning correctly and is properly calibrated (Checking electrical, mechanical, and operational functions may be independent of the procedure). The performance of daily

quality control activities may serve as an additional instrument function check, since analysis of external control samples check the operating characteristics of a test system, including instrument stability and calibration.

The laboratory must follow and document the necessary functions checks as stated by the laboratory information system (LIS) manufacturer for the LIS computer and devices such as monitors, printers and modems.

For instruments that automatically perform function checks and flag problems, the laboratory is required to document the corrective actions in response to the flagged problems. Use D5753 for deficiencies related to documenting corrective actions in response to the flagged problems.

Flow cytometry:

A fluorescence standard(s) for each fluorochrome should be used each day of patient testing to ensure:

- Proper alignment of the optical system;
- Standardization of the fluorescence detectors;
- Resolution of dimly-stained particles; and
- Appropriate compensation for spectral overlap of the fluorochromes.

Fluorescence standards should have the same fluorochromes as are used for the test, and with the exception of alignment standards, should have similar fluorescence intensities as found in the test specimens. The laboratory must have an acceptable range of performance for all procedures.

Probes §493.1254(a)(2)

For those methods in which the centrifugation is a critical portion of the test, does the laboratory check the RPM's and timing periodically (e.g., urine sediments)?

Do the records of the laboratory that moves from testing site to testing site demonstrate the performance of function checks as necessary?

In immunofluorescent test procedures, how does the laboratory assure that the bulb is emitting ultraviolet light at the correct wave length?

How does the laboratory ensure that the fluorescent light source has not exceeded the manufacturer's established optimal timeframe?

For procedures or test systems that require pipetting or dilution of patient specimens separately from controls or calibrators, how are autodiluters, microdiluters, and/or pipettors checked for adequate and consistent delivery?

For those systems that perform simultaneous fluid delivery to multi-well plates or tubes, how does the laboratory assure uniform delivery of reagents or washing solutions to all wells or tubes?

§493.1254 Standard: Maintenance and function checks.

(b) Equipment, instruments, or test systems developed in-house, commercially available and modified by the laboratory, or maintenance and function check protocols are not provided by the manufacturer. The laboratory must do the following:

Interpretive Guidelines §493.1254(b)

The laboratory must establish and follow procedures for performing maintenance and function checks on each piece of equipment/instrument it uses, including those that are peripherally involved in patient testing (e.g., incubators, centrifuges, safety cabinets, autoclaves and microscopes).

A manufacturer's instructions may not require maintenance and function checks, however, if the laboratory determines that a maintenance and/or function check protocol is necessary in order to ensure accurate and reliable test results, the laboratory must establish a maintenance protocol and perform and document the activities. Additionally, a laboratory must define the function check protocol and perform and document the function checks.

D5433

§493.1254 Standard: Maintenance and function checks.

(b)(1)(i) Establish a maintenance protocol that ensures equipment, instrument, and test system performance that is necessary for accurate and reliable test results and test result reporting.

(b)(1)(ii) Perform and document the maintenance activities specified in paragraph (b)(1)(i) of this section.

Interpretive Guidelines §493.1254(b)(1)

A laboratory's maintenance program is usually divided into two parts:

- *Unscheduled repairs when needed; and*
- *Scheduled preventive maintenance (PM) which is performed to prevent breakdowns or malfunctions, to prolong the life of an instrument and to maintain optimum operating characteristics.*

Probes §493.1254(b)(1)

How does the laboratory's maintenance program assure that instruments and equipment maintain optimum operating characteristics and minimize breakdowns?

Has the laboratory evaluated whether any modifications it has made to a manufacturer's instrument or piece of equipment has resulted in the need for additional maintenance or function checks, and, if so, have the additional procedures been established and implemented?

D5435

§493.1254 Standard: Maintenance and function checks.

(b)(2)(i) Define a function check protocol that ensures equipment, instrument, and test system performance that is necessary for accurate and reliable test results and test result reporting.

(b)(2)(ii) Perform and document the function checks, including background or baseline checks, specified in paragraph (b)(2)(i) of this section. Function checks must be within the laboratory's established limits before patient testing is conducted.

Interpretive Guidelines §493.1254(b)(2)(i)-(b)(2)(ii)

The laboratory must establish and follow procedures for performing function checks on each piece of equipment/instrument it uses, including those that are peripherally involved in patient testing (e.g., incubators, centrifuges, safety cabinets, autoclaves).

Function checks refer to those activities performed to evaluate critical operating characteristics (e.g., stray light, zeroing, electrical levels, optical alignment, background counts, counting efficiency) according to the accepted method of operation for each type of device or instrument. Daily quality control activities and function checks are performed prior to patient testing to ensure that an instrument is functioning correctly and is properly calibrated. Checking electrical, mechanical, and operational functions may be independent of the procedure. The performance of daily quality control activities serves as an additional instrument function check, since analysis of external control samples check the operating characteristics of a test system, including instrument stability and calibration.

When function checks are critical to test performance, the laboratory must have a mechanism in place to monitor such items as:

- *Rotator speed and circumference;*
- *Timers;*
- *Anaerobic chambers;*
- *Cell washers;*
- *Radioactive particle counters;*
- *Blood cell counters; and*
- *Nucleic acid amplification equipment.*

Flow cytometry:

A fluorescence standard(s) for each fluorochrome must be used each day of patient testing to ensure:

- *Proper alignment of the optical system;*
- *Standardization of the fluorescence detectors;*
- *Resolution of dimly-stained particles; and*
- *Appropriate compensation for spectral overlap of the fluorochromes.*

Fluorescence standards must have the same fluorochromes incorporated into them as are used for the test, and with the exception of alignment standards, must have similar fluorescence intensities as found in the test specimens. The laboratory must have an acceptable range of performance for all procedures.

For flow cytometers with air-cooled lasers, the laser should be tested each day patients are tested by peaking the laser signal and monitoring the current input (amps) to laser light output (milliwatts) to determine whether the brewster windows are in need of cleaning.

Probes §493.1254(b)(2)

For those methods in which the centrifugation is a critical portion of the test, how has the laboratory checked the established RPM's and timing as necessary?

In immunofluorescent test procedures, how does the laboratory assure that the bulb is emitting ultraviolet light at the correct wave length?

If function checks are not required or recommended by the manufacturer, how does the laboratory establish the performance criteria of its equipment and instruments?

For RIA testing, are backgrounds or baselines measured for each setting? For example, if the laboratory uses more than one type of isotope, at what window setting are background counts performed and recorded?

When performing flow cytometry analysis using two or more fluorochromes

simultaneously, how does the laboratory identify and adjust for "spill over" into the other fluorescence detectors?

§493.1255 Standard: Calibration and calibration verification procedures.

Calibration and calibration verification procedures are required to substantiate the continued accuracy of the test system throughout the laboratory's reportable range of test results for the test system. Unless otherwise specified in this subpart, for each applicable test system the laboratory must do the following:

Interpretive Guidelines §493.1255

For definitions of calibration and calibration verification, refer to §493.2.

For calibration and calibration verification of blood gas analysis, see §493.1267(a) through (d).

In many instances, the performance of method calibration serves to satisfy the requirement for instrument calibration. Calibration procedures are not to be confused with instrument/equipment function checks, at §493.1254.

D5437

§493.1255 Standard: Calibration and calibration verification procedures

(a) Perform and document calibration procedures--

(a)(1) Following the manufacturer's test system instructions, using calibration materials provided or specified, and with at least the frequency recommended by the manufacturer;

(a)(2) Using the criteria verified or established by the laboratory as specified in §493.1253(b)(3)--

(a)(2)(i) Using calibration materials appropriate for the test system and, if possible, traceable to a reference method or reference material of known value; and

(a)(2)(ii) Including the number, type, and concentration of calibration materials, as well as acceptable limits for and the frequency of calibration; and

(a)(3) Whenever calibration verification fails to meet the laboratory's acceptable limits for calibration verification.

Interpretive Guidelines §493.1255(a)

The calibration requirement does not apply to a variety of procedures, which include, but are not limited to:

- *Manual procedures not involving an instrument (e.g., microbiology cultures, Kirby-Bauer disk susceptibility tests, tilt-tube prothrombin time test systems, ABO group and D (Rho) typing);*
- *Microscopic procedures (e.g., KOH preparations, pinworm preparations, urine sediment analysis, all manual differential procedures, manual cytology screening procedures); and*
- *Procedures involving an instrument in which calibration is not practical, e.g., prothrombin procedures.*

Laboratories performing testing with instruments that cannot be adjusted (e.g., unit use devices), must follow the manufacturer's instructions for initial calibration and perform calibration verification as required at §493.1255(b).

The term "calibration material" has generally replaced "standard" since many instruments now use serum-based reference materials. "Calibration material" means a solution that has a known amount of analyte weighed in or has a value determined by repetitive testing using a reference or definitive test method. Calibration material may be traceable to a National Institute for Standards and Technology (NIST) Standard, if possible.

Test method calibration procedure is based on the manufacturer's recommendations and must be followed. However, if calibration proves less stable than the manufacturer's recommendation, additional calibration materials and/or more frequent calibration may be required, as established or verified by the laboratory under §493.1253(b)(3).

The actual measurement(s) taken, reactions and/or observations must be recorded.

Probes §493.1255(a)

If the laboratory calculates values for one or more calibration materials, are the calculations correct, and do the records reflect that the measured values are within the laboratory's established limits for the calibration materials?

D5439

§493.1255(b) Standard: Calibration and calibration verification procedures

(b) Perform and document calibration verification procedures—

(b)(1) Following the manufacturer's calibration verification instructions;

(b)(2) Using the criteria verified or established by the laboratory under §493.1253(b)(3)—

(b)(2)(i) Including the number, type, and concentration of the materials, as well as acceptable limits for calibration verification; and

(b)(2)(ii) Including at least a minimal (or zero) value, a mid-point value, and a maximum value near the upper limit of the range to verify the laboratory's reportable range of test results for the test system; and

(b)(3) At least once every 6 months and whenever any of the following occur:

(b)(3)(i) A complete change of reagents for a procedure is introduced, unless the laboratory can demonstrate that changing reagent lot numbers does not affect the range used to report patient test results, and control values are not adversely affected by reagent lot number changes.

(b)(3)(ii) There is major preventive maintenance or replacement of critical parts that may influence test performance.

(b)(3)(iii) Control materials reflect an unusual trend or shift, or are outside of the laboratory's acceptable limits, and other means of assessing and correcting unacceptable control values fail to identify and correct the problem.

(b)(3)(iv) The laboratory's established schedule for verifying the reportable range for patient test results requires more frequent calibration verification.

Interpretive Guidelines §493.1255(b)

If the laboratory performs a calibration protocol using 3 or more levels of calibration materials that include a low, mid, and high value at least every 6 months, the calibration verification requirement is met.

For kinetic enzymes, the calibration verification requirements may be met by verifying the procedure using a high enzyme level material such as a control, calibration material, or patient specimen and diluting it to cover the reportable range.

Control activities routinely used to satisfy the requirement for §493.1256 do not satisfy the calibration verification requirements.

EXCEPTIONS:

1. For automated cell counters, the calibration verification requirements are considered met if the laboratory follows the manufacturer's instructions for instrument operation and tests 2 levels of control materials each day of testing provided the control results meet the laboratory's criteria for acceptability.
2. If the laboratory follows the manufacturer's instruction for instrument operation and routinely tests three levels of control materials (lowest level available, mid-level, and highest level available) more than once each day of testing; the control material results meet the laboratory's criteria for acceptability and the control materials are traceable to National Institute of Standards and Technology (NIST) reference materials, the calibration verification requirements are met.

Calibration materials, proficiency testing samples with known results, or control materials with known values may be used to perform calibration verification. For these materials, the laboratory must define acceptable limits for the difference between the measured value obtained, versus the actual concentration of the materials.

If reagents are obtained from a manufacturer and all of the reagents for a test are packaged together, the laboratory is not required to perform calibration verification for each package of reagents, provided the packages of reagents are received in the same shipment and contain the same lot number.

When reviewing the laboratory's maintenance and function check records as required in §493.1254, determine whether the laboratory performed calibration verification when major maintenance occurred or critical parts were replaced.

The actual measurement(s) taken, reactions and/or observations must be recorded.

Probes §493.1255(b)

If a laboratory does not perform calibration verification after a complete change of reagents, what data does the laboratory have to document that changing reagent lot numbers does not affect the reportable range of patient test results, and does not adversely affect control results?

D5441

§493.1256 Standard: Control procedures.

- (a) For each test system, the laboratory is responsible for having control procedures that monitor the accuracy and precision of the complete analytic process.**
- (b) The laboratory must establish the number, type, and frequency of testing control materials using, if applicable, the performance specifications verified or established by the laboratory as specified in §493.1253(b)(3).**
- (c) The control procedures must--**
 - (c)(1) Detect immediate errors that occur due to test system failure, adverse environmental conditions, and operator performance.**
 - (c)(2) Monitor over time the accuracy and precision of test performance that may be influenced by changes in test system performance and environmental conditions, and variance in operator performance.**

Interpretive Guidelines §493.1256(a)-(c)

For each test system, the laboratory is responsible for monitoring the accuracy and precision of each phase of the analytic testing process by using control procedures that

will detect immediate errors and errors occurring over time. Errors may occur due to test system failure, change in environmental conditions, and operator performance.

TEST SYSTEM

Test system failures may result from reagent contamination or deterioration, reagent lot variation, reaction temperature fluctuations, inadequate sampling, improper or loss of calibration, electronic or mechanical failure, power supply variances, etc.

ENVIRONMENT

Environmental conditions that may affect test system performance include temperature, airflow, light intensity, humidity, altitude, etc.

OPERATOR

Operator performance that may affect testing include improper specimen preparation and handling, incorrect test interpretation, failure to follow the manufacturer's test system instructions, etc. Operator training prior to testing is critical and competency assessment over time is necessary to ensure continued appropriate test performance. (See subpart M)

NCCLS EP-18, "Quality Management for Unit-Use Testing," provides guidance for identifying test system, environmental, and operator sources of error. Many manufacturers adhere to this NCCLS guidance and have identified potential sources of error for their test system. Manufacturers should provide this information to their client laboratories upon request.

Interpretive Guidelines §493.1256(c)

CONTROL PROCEDURES

In determining the control procedures, including the frequency of testing controls that detect immediate errors and monitor test performance over time, the laboratory needs to consider the following:

- *Control procedures specified by the test system's manufacturer;*
- *Test system instrument and reagent stability (e.g., relocation);*
- *Frequency and volume of test performance;*
- *Technique dependence of the method;*
- *Frequency of quality control failures; and*
- *Training, experience, and competency of technical personnel.*

Traditionally, laboratories have tested two levels of external control materials daily to monitor the accuracy and precision of the analytic test system components. External control materials have a similar matrix to that of patient specimens, are treated in the same manner as patient specimens, and go through all analytic phases of testing. External control materials may be provided as part of the test system, provided separately or prepared in-house. Testing external controls meets the requirement for monitoring test system components, environment, and operator performance. External control materials may be:

- *Commercially or in-house prepared controls;*
 - *Proficiency testing specimens for which results have been confirmed;*
 - *Reference or control strains of microorganisms;*
 - *Calibrators of different lot numbers and concentration than those used to calibrate the system; or*
 - *Previously tested patient specimens provided the laboratory determines the acceptable performance level for the patient specimens.*
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D5445

§493.1256 Standard: Control procedures.

(d) Unless CMS approves a procedure, specified in Appendix C of the State Operations Manual (CMS Pub. 7), that provides equivalent quality testing, the laboratory must--

(d)(1) Perform control procedures as defined in this section unless otherwise specified in the additional specialty and subspecialty requirements at §§493.1261 through 493.1278.

(d)(2) For each test system, perform control procedures using the number and frequency specified by the manufacturer or established by the laboratory when they meet or exceed the requirements in paragraph (d)(3) of this section.

Interpretive Guidelines §493.1256(d)

Considerations for establishing equivalent quality testing

If the laboratory chooses to implement the reduced QC frequency for multiple instruments (including the same make and model used to perform the same test) a successful evaluation process must be performed for each instrument for which the (QC) frequency applies.

NOTE: *The regulations require laboratories to follow test system manufacturer's instruction for performing the testing. This means the laboratory must perform and follow the manufacturer's package insert as approved or cleared by the FDA.*

Advancements in laboratory technology have led to test systems that often include internal monitoring systems (electronic, internal, procedural controls, etc.). Electronic controls only monitor the electrical or electronic components of the test system. Internal or procedural controls may only monitor a portion of the analytic process, such as sample addition, instrument/reagents interaction, or test completion. These advancements may allow laboratories flexibility in determining control procedures that provide equivalent quality procedures to the traditional daily testing of two levels of external control materials. However, under no circumstances may the laboratory reduce the frequency of testing external control materials to less than that specified by the manufacturer's test system instructions.

NOTE: *Since the purpose of control testing is to detect immediate errors and monitor performance over time, increasing the interval between control testing (i.e., weekly, or monthly) will require a more extensive evaluation of patient test results when a control failure occurs (see §493.1282). The director must consider the laboratory's clinical and legal responsibility for providing accurate and reliable patient test results versus the cost implications of reducing the quality control testing frequency.*

Identifying Sources of Error

As a first step, the laboratory must determine the test system's sources of error. The test system instructions (product insert) may contain this information. If this information is not provided, the laboratory should contact the manufacturer to obtain this information in writing and include it in the procedure manual.

Test Systems with Internal and/or Procedural Controls

If internal or procedural controls are provided as part of the test system, the following information must be determined by the laboratory:

- *Whether the internal/procedural control(s) monitor all components of the test system. This information may be included in the package insert. If not, the laboratory must contact the test system's manufacturer to obtain written documentation identifying the components of the test system monitored by the*

internal/procedural controls and include this information in the laboratory's procedure manual;

- *If all components are not monitored, identify those components of the test system that are monitored by the internal/procedural control(s);*
- *Have a mechanism for monitoring those components of the test system not monitored by the internal/procedural control(s); and*
- *Evaluate the affect of adverse environmental conditions and the influence of operator variance and techniques.*

NOTE: *Although manufacturers may assist laboratories by providing quality control instructions, the laboratory is ultimately responsible for the performance of appropriate quality control procedures, including the documentation and interpretation of quality control data. Under subpart M, the director is responsible for ensuring that quality control (use D6020 or D6093 as appropriate) and quality assessment (use D6021 or D6094 as appropriate) programs are established and maintained to assure the quality of laboratory services, including the identification of failures in quality as they occur (use D6022 and D6094).*

Equivalent Quality Control Procedures

The equivalent quality control procedures described below **may only be used** for laboratory testing subject to the following control procedure requirements:

- §493.1256(d)(3)(i-iii) – control requirements for quantitative, qualitative and semi-quantitative procedures
- §493.1256(d)(3)(iv) -- test procedures that include an extraction phase (limited to 1 and 2 below)
- §§493.1267-493.1269 – control requirements for routine chemistry and hematology (limited to 1 and 2 below)

As further technological advances are made and additional data becomes available, CMS will, as appropriate, revise the equivalent quality control procedures and/or the eligibility requirements for test procedures that may use equivalent quality control.

1. Test Systems with Internal/Procedural Control(s) that Monitor the Entire Analytic Process

If a test system uses one or more internal/procedural control(s) to monitor all of its analytic components and the laboratory using the test system successfully completes the evaluation process described below to demonstrate test system stability over time, the laboratory may use the equivalent quality control procedures described below in lieu of performing the applicable procedures specified in the regulations at §493.1256(d)(3)(i-iv) and the applicable specialty and subspecialty requirements listed for routine chemistry and hematology at §§493.1267-493.1269.

Evaluation Process: The laboratory must perform the test system's internal control procedure(s) in accordance with the manufacturer's instructions (but not less frequently than once each day of testing) and test two levels of external control material daily for 10 consecutive days of testing.

- If the internal and external control results are acceptable throughout the evaluation process, the laboratory may reduce the frequency of testing two levels of external control material from daily to **once per calendar month unless the manufacturer requires more frequent and/or additional external control testing.** The laboratory must continue to perform and monitor the internal control(s) in accordance with the manufacturer's instructions, but not less frequently than once each day of testing.

- If any internal or external control result is unacceptable during the evaluation process or after the laboratory has reduced the frequency for testing external control materials, the laboratory must repeat the unacceptable internal and/or external control.
 - If the repeat control result(s) are within range, no further corrective action is necessary and the laboratory may, as applicable, resume the evaluation process or continue the reduced frequency of external control testing.
 - If the repeat control result(s) are not acceptable, the laboratory must identify the problem, take appropriate corrective action and follow the requirements at §493.1282(b)(2) before reporting patient test results. The laboratory must **restart** and successfully complete the evaluation process before reducing the frequency of testing external control materials.
- All evaluation process and corrective action activities must be documented.

Note: If a laboratory's existing QC data for the test system meets the evaluation process protocol described above, the laboratory may reduce the frequency for testing external control materials as specified above.

The laboratory must perform calibration verification (§493.1255), as applicable, and test external control materials (§493.1256) with each complete change of reagents, with each new lot number or shipment of reagents, following major preventive maintenance, or replacement of critical parts that may influence test performance. If the calibration verification and external control results are acceptable, the laboratory may continue monthly external control and daily internal control testing.

For each test, the following ongoing assessment activities are also required:

- Proficiency testing:
 - Results must demonstrate acceptable/satisfactory performance as specified in subpart H;
 - Acceptable performance must be demonstrated for testing for which proficiency testing is not required or proficiency testing materials are not available (§493.1236);
- Analytic system quality assessment (§493.1289) activities must demonstrate problems are not occurring; and
- Competency assessment evaluations must demonstrate testing personnel are accurately performing testing as specified in subpart M.

If unacceptable results are obtained for any of the above assessment activities, the laboratory must investigate, identify the problem, document the corrective action(s) taken, and **restart** the evaluation process.

2. Test Systems with Internal/Procedural Control(s) that Monitor a Portion of the Analytic Process

Some internal/procedural controls monitor only certain components of the test system. Although the test system's manufacturer may suggest other mechanisms to monitor the component(s) not checked by the internal/procedural controls, the laboratory is ultimately responsible for ensuring that all components of the analytic process are monitored. The laboratory may use the equivalent quality control procedures listed below in lieu of performing the applicable procedures specified in the regulations at §493.1256(d)(3)(i-iv) and the applicable specialty and subspecialty requirements listed for routine chemistry and hematology at §§493.1267-493.1269, when it can demonstrate the test system's stability over time. This may be substantiated by successfully completing the evaluation process (described below).

Evaluation Process: The laboratory must perform the test system's internal control procedure(s) in accordance with the manufacturer's instructions (but not less frequently than once each day of testing) and test two levels of external control material daily for 30 consecutive days of testing.

- If the internal and external control results are acceptable throughout the evaluation process, the laboratory may reduce the frequency of testing two levels of external control material from daily to once per calendar week unless the manufacturer requires more frequent and/or additional external control testing. The laboratory must continue to perform and monitor the internal control(s) in accordance with the manufacturer's instructions, but not less frequently than once each day of testing.
- If any internal or external control result is unacceptable during the evaluation process or after the laboratory has reduced the frequency for testing external control materials, the laboratory must repeat the unacceptable internal and/or external control.
 - If the repeat control result(s) are within range, no further corrective action is necessary and the laboratory may, as applicable, resume the evaluation process or continue the reduced frequency of external control testing.
 - If the repeat control result(s) are not acceptable, the laboratory must identify the problem, take appropriate corrective action and follow the requirements at §493.1282(b)(2) before reporting patient test results. The laboratory must restart and successfully complete the evaluation process before reducing the frequency of testing external control materials.
- All evaluation process and corrective action activities must be documented.

Note: If a laboratory's existing QC data for the test system meets the evaluation process protocol described above, the laboratory may reduce the frequency for testing external control materials as specified above.

The laboratory must perform calibration verification (§493.1255), as applicable, and test external control materials (§493.1256) with each complete change of reagents, with each new lot number or shipment of reagents, following major preventive maintenance, or replacement of critical parts that may influence test performance. If the calibration verification and external control results are acceptable, the laboratory may continue weekly external control and daily internal control testing.

For each test, the following ongoing assessment activities are also required:

- Proficiency testing:
 - Results must demonstrate acceptable/satisfactory performance as specified in subpart H;
 - Acceptable performance must be demonstrated for testing for which proficiency testing is not required or proficiency testing materials are not available (§493.1236);
- Analytic system quality assessment (§493.1289) activities must demonstrate problems are not occurring; and
- Competency assessment evaluations must demonstrate testing personnel are accurately performing testing as specified in subpart M.

If unacceptable results are obtained for any of the above assessment activities, the laboratory must investigate, identify the problem, document the corrective action(s) taken and restart the evaluation process.

3. Test Systems without Internal/Procedural Control(s)

Test systems without internal/procedural controls subject to the extraction phase control requirements at §493.1256(d)(3)(iv) or the specialty or subspecialty requirements at §§493.1261-493.1278 are not eligible for this option.

Advancements in laboratory technology have led to the production of test systems that are capable of maintaining stable performance specifications over time and are minimally influenced by adverse environmental conditions and operator variance. While the test system manufacturer should provide the laboratory with written documentation of the test system's stability (which may be included as part of the package insert or operator manual, and must be maintained by the laboratory), the laboratory is responsible for ensuring that all components of the analytic process are monitored. This may be accomplished by testing, at a minimum, two levels of external control material daily. The laboratory may use the equivalent quality control procedures described below in lieu of performing the applicable procedures specified in the regulations at 493.1256(d)(3)(i-iii),

when it can demonstrate the test system's stability over time. This may be substantiated by successfully completing the evaluation process (described below).

Evaluation Process: The laboratory must perform the test system's control procedures in accordance with the manufacturer's instructions and, at a minimum, test two levels of external control material daily for 60 consecutive days of testing. Because the test system's performance may be affected by operator variance, all personnel who will perform the test must participate in the evaluation.

- If the external control results are acceptable throughout the evaluation process, the laboratory may reduce the frequency of testing two levels of external control material from daily to once per calendar week unless the manufacturer requires more frequent and/or additional external control testing.
- If any external control result is unacceptable during the evaluation process or after the laboratory has reduced the frequency for testing external control material, the laboratory must repeat the unacceptable external control.
 - If the repeat control result(s) are within range, no further corrective action is necessary and the laboratory may, as applicable, resume the evaluation process or continue the reduced frequency of external control testing.
 - If the repeat control result(s) are not acceptable, the laboratory must identify the problem, take appropriate corrective action and follow the requirements at §493.1282(b)(2) before reporting patient test results. The laboratory must restart and successfully complete the evaluation process before reducing the frequency of testing external control materials.
- All evaluation process and corrective action activities must be documented.

Note: If a laboratory's existing QC data for the test system meets the evaluation process protocol described above, the laboratory may reduce the frequency for testing external control materials as specified above.

The laboratory must perform calibration verification (§493.1255), as applicable, and test external control materials (§493.1256) with each complete change of reagents, with each new lot number or shipment of reagents, following major preventive maintenance, or replacement of critical parts that may influence test performance. If the calibration verification and external control results are acceptable, the laboratory may continue weekly external control testing.

For each test, the following ongoing assessment activities are also required for each test:

- Proficiency testing:
 - Results must demonstrate acceptable/satisfactory performance as specified in subpart H;
 - Acceptable performance must be demonstrated for testing for which proficiency testing is not required or proficiency testing materials are not available (§493.1236);
- Analytic system quality assessment (§493.1289) activities must demonstrate problems are not occurring; and
- Competency assessment evaluations must demonstrate testing personnel are accurately performing testing as specified in subpart M.

If unacceptable results are obtained for any of the above assessment activities, the laboratory must investigate, identify the problem, document the corrective action(s) taken and **restart** the evaluation process.

§493.1256 Standard: Control procedures.

(d)(3) At least once each day patient specimens are assayed or examined perform the following for--

Interpretive Guidelines §493.1256(d)(3)

NOTE: Throughout the analytic systems section, the regulations require laboratories to follow test system manufacturer's instruction for performing the testing. This means the laboratory must perform and follow all manufacturer's recommendations and suggestions for testing as well as those that are required to be followed.

Laboratories must follow manufacturers' test system instructions for control performance and meet the requirements in this section. The laboratory must determine if more extensive (e.g., number, frequency) control testing is necessary. Use D5425.

Immunology:

Determine which immunological methods the laboratory uses and how the laboratory tests quality control materials to check each test component of the test system. Examples of test systems that have multiple components are:

- Complement Fixation (CF);
- Hemagglutination inhibition (HAI);
- Radio-immunoassay (RIA);
- Enzyme immunoassay (EIA);
- Indirect immunofluorescence (IFA);
- Fluorescence Polarization Immunoassay (FPIA);
- Radioimmunoprecipitin assay (RIPA); and
- Radioallergosorbent test (RAST).

Use D5449 or D5451, as appropriate.

Syphilis Serology:

For FTA-ABS tests, does the laboratory employ:

- Reactive control serum in Phosphatase Buffered Solution (PBS);
- Reactive control serum in sorbent;
- Minimally reactive control 1+;
- Non-specific serum control in PBS;
- Non-specific serum control in sorbent;
- Non-specific staining control of PBS; and
- Non-specific staining control of sorbent?

For MHATP or HATTS tests, does the laboratory employ:

- Reactive reference control material;
- Non-reactive reference control material;
- Unsensitized erythrocyte with each specimen;
- Unsensitized erythrocyte with buffer;
- Sensitized erythrocyte with buffer;
- Unsensitized erythrocyte with each reactive control serum; and
- Unsensitized erythrocyte with non-reactive control serum?

Use D5451.

Probes §493.1256(d):

What data does the laboratory have to support its frequency of testing quality control samples?

How does a mobile laboratory evaluate instrument and reagent stability following relocation to determine the frequency of testing quality control samples?

D5447

§493.1256 Standard: Control procedures.

(d)(3)(i) Each quantitative procedure, include two control materials of different concentrations;

Interpretive Guidelines 493.1256(d)(3)(i)

For monitoring the abnormal range, the laboratory must select controls that correlate with the patient values either in terms of specimen matrix or range to be evaluated.

Routine Chemistry:

For monitoring the abnormal range, the laboratory should select control materials that correlate with the patient values both in terms of specimen matrix and range to be evaluated. For example, an elevated serum based bilirubin control should be employed when measuring neonatal bilirubins; a low level protein control or cerebrospinal fluid control should be used for monitoring cerebrospinal fluid protein.

Hematology:

For instruments which perform hemoglobin, hematocrit, red and white blood cell counts, platelets and/or differentials, acceptable controls are 2 levels of assayed materials, OR 1 level of assayed material and 1 patient specimen that was verified in the same batch of specimens with the assayed control material. The laboratory must establish criteria for an acceptable range of performance as required at D5481.

EXCEPTION:

Unless otherwise required by the test system's manufacturer or the laboratory's performance specifications, for instruments that perform white blood cell differentials directly from blood films (smears), a commercial control or patient specimen (differential) that has been verified through repetitive testing is an acceptable control and satisfies the requirements of §493.1256(d), as appropriate.

D5449

§493.1256 Standard: Control procedures.

(d)(3)(ii) Each qualitative procedure, include a negative and positive control material;

Interpretive Guidelines §493.1256(d)(3)(ii)

Urinalysis

Photomicrographs or charts of all possible urine sediment components will meet the control requirement for manual microscopic urinalysis examinations. Use D5445.

D5451

§493.1256 Standard: Control procedures.

(d)(3)(iii) Test procedures producing graded or titered results, include a negative control material and a control material with graded or titered reactivity, respectively;

Interpretive Guidelines §493.1256(d)(3)(iii)

For tests in which patient results are reported in terms of graded reactivity (1+, 2+, 3+, etc.) control(s) of graded reactivity must be used. For tests in which patient results are reported as a titer, controls of known titer must be used.

EXCEPTIONS:

A negative control is not required for anti-streptolysin O titer, anti-hyaluronidase titer tests. A positive control is not required for the cold agglutination test. For radial immuno-diffusion, one control or calibration material is required on each plate.

D5453

§493.1256 Standard: Control procedures.

(d)(3)(iv) Each test system that has an extraction phase, include two control materials, including one that is capable of detecting errors in the extraction process; and

Interpretive Guidelines §493.1256(d)(3)(iv)

Test systems with an extraction phase(s) are not eligible for the equivalent quality testing protocol.

Bacteriology:

*For direct antigen systems, laboratories may use bacterial cell suspensions to meet the requirement for control organisms since the cell suspensions are subjected to both the extraction and reaction phases of the test. However, a matrix similar to patient specimens is preferred. For example, for direct antigen tests for group A streptococcal antigen, commercially prepared, dried (solid-shafted) swabs, one containing group A streptococcus (*S. pyogenes*) as a positive control and another with non-group A streptococcus and/or *Staphylococcus aureus* as a negative control may be used.*

Additionally, if the manufacturer's instructions do not specify what the positive control contains, the laboratory should contact the manufacturer to ensure that the positive control contains a cell suspension of the organism. Otherwise, the laboratory must have an alternative mechanism for meeting this requirement (e.g., laboratory suspension stock ATCC organism, commercially prepared organism controls).

Toxicology:

For gas chromatography and mass spectrometry used for drug confirmations, an analyte specific control is required for both qualitative and quantitative tests.

For comprehensive broad spectrum qualitative drug screening procedures using gas chromatography, a control material containing one or more drugs representative of each drug class reported [e.g., tricyclic antidepressants, barbiturates must go through each test phase, including the extraction process.

D5455

§493.1256 Standard: Control procedures.

(d)(3)(v) Each molecular amplification procedure, include two control materials and, if reaction inhibition is a significant source of false negative results, a control material capable of detecting the inhibition.

Interpretive Guidelines §493.1256(d)(3)(iii)

The laboratory is also responsible for following the manufacturer's instructions concerning procedure limitations for detecting nucleic acid target amplification sequences, when provided by the manufacturer.

If the laboratory suspects the presence of interfering substances (inhibitors), the laboratory is responsible for using a control material (in addition to positive and negative control materials) capable of detecting interfering substances. Patient specimens may contain substances (inhibitors) that interfere with the enzymatic reaction of a molecular amplification procedure. These interfering substances could affect the assay's sensitivity causing a false negative result. Interfering substances may include, but are not limited to components within the patient specimen or

exogenous substances introduced during the preanalytic and/or analytic phase of testing.

D5457

§493.1256 Standard: Control procedures.

(d)(4) For thin layer chromatography--

(d)(4)(i) Spot each plate or card, as applicable, with a calibrator containing all known substances or drug groups, as appropriate, which are identified by thin layer chromatography and reported by the laboratory; and

(d)(4)(ii) Include at least one control material on each plate or card, as applicable, which must be processed through each step of patient testing, including extraction processes.

Interpretive Guidelines §493.1256(d)(4)

For qualitative urine drug screens performed by thin layer chromatography, a negative control is not required. However, a control containing one or more drugs representative of each drug group reported (e.g., tricyclic antidepressants, barbiturates) that goes through each test phase (including the extraction process) is required.

D5459

§493.1256 Standard: Control procedures.

(d)(5) For each electrophoretic procedure include, concurrent with patient specimens, at least one control material containing the substances being identified or measured.

D5461

§493.1256 Standard: Control procedures.

(d)(6) Perform control material testing as specified in this paragraph before resuming patient testing when a complete change of reagents is introduced; major preventive maintenance is performed; or any critical part that may influence test performance is replaced.

D5463

§493.1256 Standard: Control procedures.

(d)(7) Over time, rotate control material testing among all operators who perform the test.

Interpretive Guidelines §493.1256(d)(7)

The laboratory may use this requirement to assist in competency assessment determinations specified in subpart M.

D5465

§493.1256 Standard: Control procedures.

(d)(8) Test control materials in the same manner as patient specimens.

Interpretive Guidelines §493.1256(d)(8)

Control materials of a similar matrix to that of patient specimens should be utilized, if available, and the control materials must be treated in the same manner as patient specimens and go through all analytic test phases.

Flow Cytometry

In cell surface phenotyping by flow cytometry or fluorescent microscopy, control samples must be analyzed within the same time period after staining as test specimens.

Probes §493.1256(d)(8)

Flow Cytometry

How did the laboratory establish the time period in which stained cells must be analyzed to avoid significant loss of any cell subpopulations or total cell numbers?

If analysis will be based on a population of cells selected by flow cytometry "gating" on size or density parameters, or selected by depletion or enrichment techniques, are controls tested with each patient to detect the presence of contaminating cells in the selected population? (e.g., Monocyte contamination of "lymphocytes" gated by forward angle or forward angle versus 90° light scatter must be detected with a monocyte-specific antibody.) Use D5465 or D5425 as appropriate.

D5467

§493.1256 Standard: Control procedures.

(d)(9) When using calibration material as a control material, use calibration material from a different lot number than that used to establish a cut-off value or to calibrate the test system.

D5469

§493.1256 Standard: Control procedures.

(d)(10) Establish or verify the criteria for acceptability of all control materials.

(d)(10)(i) When control materials providing quantitative results are used, statistical parameters (for example, mean and standard deviation) for each batch and lot number of control materials must be defined and available.

(d)(10)(ii) The laboratory may use the stated value of a commercially assayed control material provided the stated value is for the methodology and instrumentation employed by the laboratory and is verified by the laboratory.

(d)(10)(iii) Statistical parameters for unassayed control materials must be established over time by the laboratory through concurrent testing of control materials having previously determined statistical parameters.

Interpretive Guidelines §493.1256(d)(10)

Acceptable ranges must be verified (assayed) or established (unassayed) by the laboratory for control materials and any calibrators that are used in lieu of control materials.

For procedures in which a spiked sample is used as a control, an acceptable range must be established for the amount of recovery of the spiked sample, either in percentage or actual concentration.

If laboratories rely on commercial companies to establish statistical limits for controls, the laboratory must have documentation to verify that its control results correlate with the

established limits.

When patient specimens are used to meet the control requirements, data must be evaluated in accordance with §493.1256(d)(10)(iii).

There are no specific guidelines for the number of times a material must be tested to establish statistical limits. In general, twenty replicate tests should be considered the minimum for determining a standard deviation.

Probes §493.1256(d)(10)

What statistics does the laboratory have to demonstrate the number of assays and the period of time in which the laboratory repetitively tested control materials to verify or establish control limits?

How does the laboratory evaluate control results to detect any outliers, shifts or trends in control values due to instrument malfunctions or changes in the analytical system?

If more than one test system is in use for a test procedure, did the laboratory evaluate the data for each test method in the establishment of control limits?

§493.1256 Standard: Control procedures.

(e) For reagent, media, and supply checks, the laboratory must do the following:

D5471

§493.1256 Standard: Control procedures.

(e)(1) Check each batch (prepared in-house), lot number (commercially prepared) and shipment of reagents, disks, stains, antisera, (except those specifically referenced in §493.1261 (a)(3)) and identification systems (systems using two or more substrates or two or more reagents, or a combination) when prepared or opened for positive and negative reactivity, as well as graded reactivity, if applicable.

Interpretive Guidelines §493.1256(e)(1)

Review the laboratory's quality control records and note when lot numbers change.

NOTE: Media checks are defined under §493.1256(e)(4) Guidelines.

The laboratory must demonstrate that each reagent performs within the specifications established by the laboratory for the test procedure. Documentation of concurrent testing of reagents or acceptable quality control results will satisfy this requirement.

Reagents, disks, and test procedures used for identification purposes may include, but are not limited to, catalase, coagulase plasma, oxidase, bacitracin, optochin, Cefinase™, ONPG, X and V factor strips and disks, germ tube, yeast morphology media, and commercial identification systems.

A negative reactivity control is not required for the mycology germ tube test.

Test each batch, lot, and shipment for positive and negative reactivity for reagents such as:

- Bacitracin;
- Catalase;
- Cefinase;
- Coagulase plasma;
- ONPG;
- Optochin;
- Oxidase;
- Spot indole; and
- X and V factor strips and disks.

For bacteriology, XV discs or strips need only be checked with an organism that produces a positive reaction.

Probes §493.1256(e)(1)

What records does the laboratory have to demonstrate that controls are tested when shipments of reagents, discs, stains, antisera or identification systems are opened or when the laboratory prepares these materials? Use D5471 for not recording performance and for nonperformance of quality control checks, and stain checks.

D5473

§493.1256 Standard: Control procedures.

(e)(2) Each day of use (unless otherwise specified in this subpart), test staining materials for intended reactivity to ensure predictable staining characteristics. Control materials for both positive and negative reactivity must be included, as appropriate.

Interpretive Guidelines §493.1256(e)(2)-(e)(3)

Acid-fast stains must be checked each day of use for positive and negative reactivity.

D5475

§493.1256 Standard: Control procedures.

(e)(3) Check fluorescent and immunohistochemical stains for positive and negative reactivity each time of use.

Interpretive Guidelines §493.1256(e)(3)

All fluorescent stains, including fluorochrome acid-fast stains, must be tested for positive and negative reactivity each time of use.

Flow Cytometry

Staining controls for cell surface immunophenotyping by flow cytometry should consist of either normal, cultured or abnormal cells known to be positive for selected standard antigens and must verify the proper performance of reagents. Frozen or other preserved cells may be used. A negative reagent control must be run for each test cell preparation, and is to consist of monoclonal antibody(ies) of the same species and isotype. Negative reagent controls will consist of:

- *For indirect stains, an irrelevant primary antibody, if available, and in all cases, the same secondary antibody(ies) conjugated with the same fluorochrome(s) used in all relevant test combinations; and*
- *For direct stains, an irrelevant antibody conjugated to the same fluorochrome and at the same fluorochromes:protein ratio used in all relevant test combinations.*

Probes §493.1256(e)(3)

For flow cell cytometric surface immunophenotyping, is a negative reagent control used to define a threshold for positive staining cells? If not, how does the laboratory define the threshold for positive staining cells?

D5477

§493.1256 Standard: Control procedures.

(e)(4) Before, or concurrent with the initial use--

(e)(4)(i) Check each batch of media for sterility if sterility is required for testing;

(e)(4)(ii) Check each batch of media for its ability to support growth and, as appropriate, select or inhibit specific organisms or produce a biochemical response; and

(e)(4)(iii) Document the physical characteristics of the media when compromised and report any deterioration in the media to the manufacturer.

Interpretive Guidelines §493.1256(e)(4)

A batch of media (solid, semi-solid, or liquid) consists of all tubes, plates, or containers of the same medium prepared at the same time and in the same laboratory; or, if received from an outside source or commercial supplier, consists of all of the plates, tubes or containers of the same medium that have the same lot numbers and are received in a single shipment.

A sample from each batch of media is sufficient as a check for:

- Sterility, if it is autoclaved or filtered during preparation;
- Ability to support growth, using at least one organism to demonstrate the ability of the media to support growth;
- Selectivity and/or inhibition, using at least one organism to confirm its selective characteristic, and at least one organism to confirm its inhibitory characteristic; and
- Biochemical response, using at least one organism which will produce the expected reaction (positive control) and with at least one organism which will not produce the expected reaction (negative control).

EXCEPTION:

A laboratory using commercially prepared microbiological culture media that is quality controlled in accordance with the NCCLS Approved Standard (M22-A2) Table 2*** need not perform quality control checks for sterility, growth, selectivity and/or inhibition and biochemical responses provided:

- The laboratory has documentation on the media label or brochure that the quality control practices conform to NCCLS specifications; and
- The laboratory documents receipt and condition of each batch of media, and notifies the media manufacturer of:
 - Cracked petri dishes;
 - Unequal filling of plates;
 - Cracked media in plates;
 - Hemolysis;
 - Freezing;
 - Excessive number of bubbles; and
 - Contamination.
 -

This exception does not apply to:

- *Campylobacter* agar;
- Chocolate agar;

- *Media for the selective isolation of pathogenic Neisseria;*
- *Other media not listed on Table 2 (e.g., dermatophyte test medium);*
- *Media used for the isolation of parasites, viruses, mycoplasmas, chlamydia;*
- *Mueller-Hinton media used for antimicrobial susceptibility tests; or*
- *Media commercially prepared and packaged as a unit or system consisting of two or more different substrates, primarily used for microbial identification.*

Although Campylobacter medium, chocolate agar and media for the selective isolation of pathogenic Neisseria are listed on Table 2, these media must be retested by the user laboratory because these media have demonstrated higher failure rates.

American Type Culture Collection (ATCC) control organisms are not necessarily required. However, if the laboratory uses "in-house" isolates for control organisms, it must have established reactivity for each organism. Use D5469.

*Central laboratories that prepare media for satellite locations must either perform the same quality control checks required of commercial manufacturers listed on Table 2*** of the NCCLS Approved Standard (M22-A2) and furnish documentation of media quality control checks to each satellite location, or each laboratory must continue to perform media checks as required under §493.1256(e)(1).*

If a laboratory screens cultures for growth or no growth, reports "No growth" and refers all growth to a reference laboratory, the screening laboratory must perform applicable quality control of the media.

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Table 2. Manufacturers' Quality Assurance Procedure for Commercially Prepared Media

Medium	Atmosphere, Length of Incubation ¹	Control Organisms (ATCC No.) ²	Expected Results
Anaerobic sheep blood and laked blood agar media (non-selective)	Anaerobic, 24–48 h	<i>B. fragilis</i> (25285) <i>C. perfringens</i> (13124) <i>F. nucleatum</i> (25586) <i>P. anaerobius</i> (27337)	Growth Growth, beta hemolysis Growth Growth
Anaerobic broths - see Thioglycollate medium			
Blood Agar-nonselective sheep blood agar media	Aerobic or CO ₂ , 24 h	<i>S. pyogenes</i> (19615) <i>S. pneumoniae</i> (6305) <i>S. aureus</i> (25923) <i>E. coli</i> (25922)	Growth, beta hemolysis Growth, alpha hemolysis Growth Growth
Blood Agar-CAMP Test (TSA with sheep blood only)	Aerobic, 24 h	<i>S. aureus</i> (33862) or <i>S. aureus</i> (25923) <i>S. agalactiae</i> (12386) <i>S. pyogenes</i> (19615)	Positive reaction (arrowhead area of clearing) Negative reaction (no arrowhead formation)
Blood Agar-Selective sheep blood agar media (Columbia CNA Agar, phenylethyl alcohol agar)	Columbia CNA CO ₂ , 24–48h	<i>S. pyogenes</i> (19615) <i>S. pneumoniae</i> (6305) <i>S. aureus</i> (25923) <i>P. mirabilis</i> (12453)	Growth, beta hemolysis Growth, alpha hemolysis Growth Inhibition (partial)
	Phenylethyl alcohol agar CO ₂ , 24–48h	<i>S. pyogenes</i> (19615) <i>S. aureus</i> (25923) <i>P. mirabilis</i> (12453)	Growth Growth Inhibition (partial)
Blood culture media (This applies to BHI, TSB, and Thiol-based media. Other media for blood culture are exempt from user performance testing provided that manufacturers certify that additional organisms appropriate for their intended use have been tested.)	Anaerobic (nonvented) within 5 days	<i>B. fragilis</i> (25285) <i>S. pneumoniae</i> (6305)	Growth Growth
	Aerobic (vented) within 5 days	<i>P. aeruginosa</i> (27853) <i>S. pneumoniae</i> (6305)	Growth Growth
Campylobacter agar (User quality control required.)	Reduced O ₂ , enriched with CO ₂ , 42 °C, 48 h	<i>C. jejuni</i> (33291) <i>E. coli</i> (25922)	Growth Inhibition (partial)

Table 2. Manufacturers' Quality Assurance Procedure for Commercially Prepared Media (Continued)

Medium	Atmosphere, Length of Incubation ¹	Control Organisms (ATCC No.) ²	Expected Results
Chocolate agar	CO ₂ , 24 and 48 h	<i>N. gonorrhoeae</i> (43069 or 43070) <i>H. influenzae</i> (10211)	Growth Growth
CIN Agar	Aerobic, 24–48 h 25 °C	<i>Y. enterocolitica</i> (9610) <i>E. coli</i> (25922) <i>P. aeruginosa</i> (27853) <i>E. faecalis</i> (29212)	Growth; deep red center, transparent border (bull's eye) Inhibition (partial to complete) Inhibition (partial to complete) Inhibition (partial to complete)
CLED Agar	Aerobic, 24–48 h	<i>E. coli</i> (25922) <i>P. vulgaris</i> (8427) <i>S. aureus</i> (25923)	Growth; yellow centers Growth; bluish, spreading inhibited (partial) Growth; uniform deep yellow
CYE/BCYE Agar	Aerobic, 48–72 h	<i>L. pneumophila</i> (33152) <i>L. bozemanii</i> (33217)	Growth; yellow-green fluorescence under long-wave u.v. light Growth; blue-white fluorescence under long-wave u.v. light
Enrichment broths for enterics (GN Broth, Selenite Broths)	Aerobic, up to 24 h	<i>S. typhimurium</i> (14028) <i>S. sonnei</i> (9290) <i>E. coli</i> (25922)	Growth on subculture Growth on subculture (may be inhibited by Selenite media) Inhibition (partial to complete) on subculture. Growth on subculture from GN broth
Eosin methylene blue media (Levine EMB Agar; EMB Agar, modified)	Aerobic, 24 h	<i>S. typhimurium</i> (14028) <i>E. coli</i> (25922) <i>E. faecalis</i> (29212)	Growth, colorless to amber colonies Growth, blue-black colonies w/green metallic sheen Inhibition (partial)
Hektoen enteric agar	Aerobic, 24 h	<i>S. typhimurium</i> (14028) <i>S. flexneri</i> (12022) <i>E. faecalis</i> (29212) <i>E. coli</i> (25922)	Growth, colonies blue to green-blue with black centers Growth, colonies green to blue-green Inhibition (partial; colonies yellow) Inhibition (partial to complete; colonies yellow to salmon colored)
MacConkey agar	Aerobic, 24 h	<i>E. coli</i> (25922) <i>P. mirabilis</i> (12453) <i>S. typhimurium</i> (14028) <i>E. faecalis</i> (29212)	Growth, pink colonies Growth, colorless colonies, inhibition of swarming (partial) Growth, colorless colonies Inhibition (partial)
Mannitol salt agar	Aerobic, 24 and 48 h	<i>S. aureus</i> (25923) <i>S. epidermidis</i> (12228) <i>P. mirabilis</i> (12453)	Growth, colonies have yellow zones at 48 h Growth, colonies have red zones at 48 h Inhibition (partial)

Table 2. Manufacturers' Quality Assurance Procedure for Commercially Prepared Media (Continued)

Medium	Atmosphere, Length of Incubation ¹	Control Organisms (ATCC No.) ²	Expected Results
Mycobacteria agar media (Lowenstein–Jensen and Middlebrook)	CO ₂ up to 21 days	<i>M. tuberculosis</i> H37Ra (25177) <i>M. kansasii</i> Group I (12478) <i>M. scrofulaceum</i> Group II (19981) <i>M. intracellulare</i> Group III (13950) <i>M. fortuitum</i> Group IV (6841) <i>E. coli</i> (25922)	Growth Growth Growth—May be inhibited on selective L-J and selective Middlebrook media Growth—May be inhibited on selective L-J and selective Middlebrook media Growth Inhibition (partial to complete)—Use only for selective mycobacteria media
Sabouraud dextrose agar	Aerobic, up to 7 days 25–35 °C	<i>C. albicans</i> (60193 or 10231) <i>T. mentagrophytes</i> (9533)	Growth Growth
Salmonella–Shigella (SS) agar	Aerobic, 24 h	<i>S. typhimurium</i> (14028) <i>S. flexneri</i> (12022) <i>E. faecalis</i> (29212) <i>E. coli</i> (25922)	Growth, colonies colorless with or without black centers Growth, colorless colonies Inhibition (complete) Inhibition (partial to complete; colonies pink to rose-red with precipitate)
Selective mycology media (media containing cycloheximide and chloramphenicol, excluding inhibitory mold agar)	Aerobic, up to 7 days 25 °C	<i>A. niger</i> (16404) <i>C. albicans</i> (10231) <i>T. mentagrophytes</i> (9533) <i>E. coli</i> (25922)	Inhibition (partial to complete) on media containing cycloheximide Growth Growth Inhibition (partial to complete) on media containing chloramphenicol
Selective media for pathogenic <i>Neisseria</i> spp. (User quality control required.)	CO ₂ , 24–48 h	<i>N. gonorrhoeae</i> (43069 or 43070) <i>N. meningitidis</i> (13090) ³ <i>P. mirabilis</i> (43071) <i>E. coli</i> (25922) ³ <i>N. sicca</i> (9913) ³ <i>C. albicans</i> (60193) ³ <i>S. epidermidis</i> (12228)	Growth Growth Inhibition (partial)—use only for media containing trimethoprim Inhibition (partial) Inhibition (partial) Inhibition (partial) Inhibition (partial)
Selective media for enterococci, with azide	Aerobic, 24 and 48 h	<i>E. faecalis</i> (29212) <i>S. pyogenes</i> (19615) <i>E. coli</i> (25922)	Growth, blackening around colonies Inhibition (partial to complete) Inhibition (partial)—Colorless colonies on bile esculin agar
Selective media for enterococci, without azide	Aerobic, 24 and 48 h	<i>E. faecalis</i> (29212) <i>S. pyogenes</i> (19615)	Growth, blackening around colonies Inhibition (partial to complete)
Thioglycolate medium, with or without indicator	Aerobic, 48 h (tightened cap)	<i>B. fragilis</i> (25285) <i>S. aureus</i> (25923)	Growth Growth
Thioglycolate medium, enriched with vitamin K and hemin	Aerobic, 48 h (tightened cap)	<i>P. anaerobius</i> (27337) <i>B. vulgatus</i> (8482) <i>C. perfringens</i> (13124)	Growth Growth Growth

Table 2. Manufacturers' Quality Assurance Procedure for Commercially Prepared Media (Continued)

Medium	Atmosphere, Length of Incubation ¹	Control Organisms (ATCC No.) ²	Expected Results
Tubed media (BHI and Tryptic Soy Broth)	Aerobic, 24-48 h	<i>E. coli</i> (25922) <i>S. aureus</i> (25923)	Growth Growth
XLD (xylose lysine desoxycholate) Agar	Aerobic, 24 h	<i>S. typhimurium</i> (14028) <i>S. flexneri</i> (12022) <i>E. faecalis</i> (29212) <i>E. coli</i> (25922)	Growth—Colonies red with black centers Growth—Colonies red Inhibition (partial) Inhibition (partial to complete; colonies yellow to yellow-red)

¹Temperature is 35 °C unless otherwise specified.

²ATCC is a registered trademark of the American Type Culture Collection.

³Required for commercial manufacturers; not necessary for testing by users.

D5479

§493.1256 Standard: Control procedures.

(e)(5) Follow the manufacturer's specifications for using reagents, media, and supplies and be responsible for results.

NOTE: Throughout the analytic systems section, the regulations require laboratories to follow test system manufacturer's instruction for performing the testing. This means the laboratory must perform and follow all manufacturer's recommendations and suggestions for testing as well as those that are required to be followed.

D5481

§493.1256 Standard: Control procedures.

(f) Results of control materials must meet the laboratory's and, as applicable, the manufacturer's test system criteria for acceptability before reporting patient test results.

§493.1256 Standard: Control procedures.

(g) The laboratory must document all control procedures performed.

*Interpretive Guidelines §493.1256(g)
The actual measurement(s) taken, reactions and/or observations must be recorded.*

D5485

§493.1256 Standard: Control procedures.

(h) If control materials are not available, the laboratory must have an alternative mechanism to detect immediate errors and monitor test system performance over time. The performance of alternative control procedures must be documented.

*Interpretive Guidelines §493.1256(h)
Laboratories may choose to split samples for testing by another method or in another laboratory to evaluate the results obtained. Previously tested patient specimens (include specimens across the reportable range) tested in duplicate. Precision is determined through replicate testing of a previously tested patient specimen. The duplicate tests may be performed by the same individual or by different people and the results compared to previously defined acceptable limits for differences between duplicates.*

PUBLIC HEALTH LABORATORIES PERFORMING NEWLY DEVELOPED ASSAYS/TEST SYSTEMS FOR AGENTS FOR EMERGENT PUBLIC HEALTH SIGNIFIANCE Screening and confirmation methods for agents of emergent public health significance require the rapid development and transfer of technology and expertise from federal agencies to public health laboratories (or other designee laboratories). Because of unique situations of emergent diseases or other public health threats, control and calibration materials for the assay or test system may not be immediately available. Under these circumstances, the laboratory must follow the assay or test system's protocol(s) without modification and document the alternative mechanisms employed to

ensure accurate test results. Laboratories are encouraged to use multiple mechanisms (as described below) for ensuring accuracy.

When control and calibration materials are not available, examples of alternative control procedures that may be available include, but not limited to, the following:

- *Split specimens for testing by another method or in another laboratory;*
- *Include previously tested patient specimens (both positive and negative) tested in duplicate as surrogate controls;*
- *Test each patient specimen in duplicate;*
- *Test multiple specimen types from the same patient (e.g., saliva, urine, serum);*
- *Perform serial dilutions of positive specimens to confirm positive reactions;*
- *Provide additional supervisory review of results prior to release.*

As soon as control and calibration materials become available, the applicable requirements in §493.1256 must be met.

For specific information regarding testing for agents of emergent public health significance and alternative methods/procedures for ensuring accuracy of this testing, refer to www.aphl.org.

Probes §493.1256(h)

If control materials are not provided by the manufacturer, how does the laboratory assure the validity of test results?

D3000

(Rev. 32, 02-143-2004)

Subpart J--Facility Administration for Nonwaived Testing

§493.1100 Condition: Facility administration.

Each laboratory that performs nonwaived testing must meet the applicable requirements under §§493.1101 through 493.1105, unless HHS approves a procedure that provides equivalent quality testing as specified in Appendix C of the State Operations Manual #7.

Interpretive Guidelines §493.1100

To determine which tests are categorized as waived or nonwaived (i.e., moderate or high complexity tests), refer to the "Specific List For Categorization of Laboratory Test Systems, Assays, and Examinations by Complexity" [www.fda.gov/cdrh/clia/index.html]. Test systems, assays, and examinations not yet classified are considered high complexity.

Significant deficiencies cited under this condition may also indicate deficiencies under personnel responsibilities.

§493.1101 Standard: Facilities.

(a) The laboratory must be constructed, arranged, and maintained to ensure the following:

D3001

§493.1101 Standard: Facilities.

(a)(1) The space, ventilation, and utilities necessary for conducting all phases of the testing process.

Interpretive Guidelines §493.1101(a)(1)

Work areas should be arranged to minimize problems in specimen handling, examination and testing of specimens, and reporting of test results.

Workbench space should be sufficient for test performance, well lit, and have water, gas, suction, and, electrical outlets as necessary. Instruments, equipment, and computer systems should be placed in locations where their operation is not affected adversely by physical or chemical factors, such as heat direct sunlight, vibrations, power fluctuations or fumes from acid or alkaline solutions. Equipment tops should not be used as workbench space.

Determination of proper lighting is subjective since the regulations do not specify the foot-candles or other measures of light intensity required. Ensure that lighting or background is appropriate for visual interpretation of test results (e.g., macroscopic evaluation of hemagglutination reactions or strep screen; dark background with reflected light for reading K-B disk diffusion AST). When citing deficiencies, document the circumstances in which lighting adversely or may adversely affect test performance or personnel safety.

Determine that the laboratory has a system to ensure its ventilation system properly removes vapors, fumes, and excessive heat, when appropriate, for the type of testing done in the laboratory.

Ensure that an adequate, stable electrical source is maintained at each location (e.g., outlets, not extension cords) and meets the power requirements for each piece of equipment.

D3003

§493.1101 Standard: Facilities.

(a)(2) Contamination of patient specimens, equipment, instruments, reagents, materials, and supplies is minimized.

D3005

§493.1101 Standard: Facilities.

(a)(3) Molecular amplification procedures that are not contained in closed systems have a uni-directional workflow. This must include separate areas for specimen preparation, amplification and product detection, and, as applicable, reagent preparation.

Interpretive Guidelines §§493.1101(a)(2)-(a)(3)

The laboratory should establish contamination prevention procedures to minimize contamination of patient specimens, equipment, instruments, reagents, materials, and supplies.

Determine if the laboratory performs wipe tests of areas where radioactive material or amplification procedures are used in order to monitor and prevent contamination.

Determine that the processing of mycobacteriology cultures is performed in a manner that prevents contamination of the environment.

Laboratories performing molecular amplification procedures should have a mechanism to detect cross-contamination of patient specimens. This may be accomplished by including a “blank” control with each run of patient specimen testing (use D5425).

Uni-directional workflow refers to the manner in which testing personnel and patient specimens move through the molecular testing process to prevent cross-contamination, and consists of separate areas for the following:

- *Reagent preparation (as applicable);*
- *Pre-amplification area for specimen preparation and amplification reaction set up;*
and
- *Post-amplification area for specimen amplification and product detection.*

Reagents must be prepared in an area that is separate (as applicable) from where specimens are processed, prepared, “amplified” and detected to prevent contamination. Once a specimen enters the amplification and product detection area it should not be brought back to the reagent or specimen preparation areas. The laboratory should store amplified specimens separately from test reagents and patient specimens. All equipment (e.g., reagents, supplies, pens, pipettes and tips, laboratory coats) should remain in designated areas.

Sources of potential cross-contamination in molecular testing include:

- *Patient specimen (i.e., genomic contamination);*
- *Amplified patient specimen (i.e., amplicon contamination); and*
- *Testing personnel.*

D3007

§493.1101 Facilities

(b) The laboratory must have appropriate and sufficient equipment, instruments, reagents, materials, and supplies for the type and volume of testing it performs.

Interpretive Guidelines §493.1101(b)

Base deficiencies related to inappropriate or insufficient equipment on a determination that patient results are or may be adversely affected. Ensure that the laboratory has the appropriate equipment to prepare reagents, stains, solutions, controls, and calibration materials (e.g., pipettes, hydrometers, graduated cylinders, autoclaves, balances, centrifuges, distilled/deionized water). If the equipment or instrumentation is found to be inappropriate or insufficient, document the reasons for this finding.

Ensure that the laboratory has test systems, equipment and/or instruments capable of producing results within the laboratory's stated test performance specifications.

Ensure that the laboratory has test systems, equipment and/or instruments necessary to perform the laboratory's volume of testing (preanalytic, analytic, postanalytic) within established turnaround times.

Data capacity in the laboratory's information system should be sufficient for current data entry. If capacity is maintained by deletion of data, it should be scheduled and documented.

For Cytology, laboratories should use coverslips that cover the entire surface of the specimen.

D3009

§493.1101 Standard: Facilities.

(c) The laboratory must be in compliance with applicable Federal, State, and local laboratory requirements.

Interpretive Guidelines §493.1101(c)

The laboratory must possess a current license issued by the State or local government, if such licensing exists. If a State or local government removes a laboratory's license and the right to operate within the State or locality, Centers for Medicare and Medicaid Services (CMS) may take an action to revoke the Clinical Laboratory Improvement Amendments (CLIA) certificate.

D3011

§493.1101 Standard: Facilities.

(d) Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials.

Interpretive Guidelines §493.1101(d)

If you observe or obtain information regarding potential safety violations not applicable under CLIA, notify the appropriate State or local authority. Consult with the Regional

Office (RO) for notification to other Federal agencies such as the Occupational Safety and Health Administration (OSHA) www.osha.gov, Environmental Protection Agency (EPA) www.epa.gov, or Nuclear Regulatory Commission (NRC). The appropriate Federal, State or local authority, if warranted, will investigate and, if necessary, conduct an on-site visit.

Probes §493.1101(d)

What safety protocols are observed and practiced in the laboratory?

How does the laboratory, including temporary testing sites or mobile units:

- Dispose of radiological, chemical, and biological wastes (including blood drawing equipment);
- Clean up spills (chemical, biological, and radiological); and
- Determine the amount of waste that can safely be contained and the precautions necessary to ensure that liquid waste does not spill or splash while in travel status?

What chemical, radiological, or biological precautions are taken, if any, during the preparation or handling of reagents?

D3013

§493.1101 Standard: Facilities.

(e) Records and, as applicable, slides, blocks, and tissues must be maintained and stored under conditions that ensure proper preservation.

Interpretive Guidelines §493.1101(e)

The laboratory must arrange a secure area for storage of records and, as applicable, slides, blocks, and tissues that will provide conditions that ensure proper preservation of specimens and records.

Paraffin blocks must be stored in a cool dry environment. Exposure to excessive heat may cause blocks to melt.

Probes §493.1101(e)

For Cytology and Histology, how does the laboratory ensure that the slides have completely dried prior to being stored?

D3015

§493.1103 Standard: Requirements for transfusion services.

A facility that provides transfusion services must meet all of the requirements of this section and document all transfusion-related activities.

Interpretive Guidelines §493.1103

A "facility that provides transfusion services" is any entity that may store and/or administer blood and blood products to patients.

D3017

§493.1103 Standard: Requirements for transfusion services.

(a) Arrangement for services. The facility must have a transfusion service agreement reviewed and approved by the responsible party(ies) that govern the procurement, transfer, and availability of blood and blood products.

Interpretive Guidelines §493.1103(a)

Determine which services are provided directly by the facility and which are provided through agreement and ensure that the agreement is being met.

D3019

§493.1103 Standard: Requirements for transfusion services.

(b) Provision of testing. The facility must provide prompt ABO grouping, D (Rho) typing, unexpected antibody detection, compatibility testing, and laboratory investigation of transfusion reactions on a continuous basis through a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by CMS.

Interpretive Guidelines §493.1103(b)

Review the agreement and determine if the outside laboratory is CLIA-certified or equivalent, as determined by CMS. An equivalent laboratory is a Veterans Administration (VA) laboratory, a CLIA-exempt laboratory or a laboratory under the auspices of the Department of Defense (DoD).

D3021

§493.1103 Standard: Requirements for transfusion services.

(c) Blood and blood products storage and distribution.

(c)(1) If a facility stores or maintains blood or blood products for transfusion outside of a monitored refrigerator, the facility must ensure the storage conditions, including temperature, are appropriate to prevent deterioration of the blood or blood product.

Interpretive Guidelines §493.1103(c)(1)

Determine where blood and blood products are stored. There may be various unconventional blood storage areas such as operating rooms, nursing stations, long-term care facilities, and dialysis units. Determine that the facility ensures the appropriate temperature is maintained and documented for each storage area during the time blood and blood products are stored.

Acceptable temperature ranges must be established and actual readings of temperature-controlled storage areas must be recorded during the time that blood or blood products for transfusion are stored. Whole Blood, Red Blood Cells, and Liquid Plasma should be stored between 1 and 6°C; room temperature Platelets and Platelet Rich Plasma between 20 and 24°C or 1-6°C as indicated on the product label. Fresh Frozen Plasma, Plasma, and Cryoprecipitated AHF should be stored at -18°C or colder.

Facilities that provide transfusion services (not certified for the specialty of Immunohematology) and perform nonwaived testing are held to the requirements for the storage and distribution of blood and blood products. The laboratory providing the blood or blood products may supply these facilities with the following:

- *Policies for the proper storage and transportation of blood or blood products;*
- *Procedures to alert the laboratory of blood storage problems;*

- Policies to ensure the positive identification of a blood or blood product recipient (use D3023);
- Procedures to identify a possible transfusion reaction (use D3025); and
- Procedures to notify the laboratory of a possible transfusion reaction (use D3025).

Determine how the appropriate temperatures of blood storage areas are maintained during a power failure.

Probes §493.1103(c)(1)

If frozen blood products are stored, how does the facility ensure products are maintained at appropriate temperatures to prevent thawing and re-freezing of the products?

D3023

§493.1103 Standard: Requirements for transfusion services.

(c)(2) The facility must establish and follow policies to ensure positive identification of a blood or blood product recipient.

Interpretive Guidelines §493.1103(c)(2)

Review the facility's policies for ensuring positive identification of blood or blood products and the intended recipient.

When possible, observe the actual practice, including issuing the blood and blood products to the intended recipient. This includes proper verification of patient identification prior to initiation of the transfusion.

D3025

§493.1103 Standard: Requirements for transfusion services.

(d) Investigation of transfusion reactions. The facility must have procedures for preventing transfusion reactions and when necessary, promptly identify, investigate, and report blood and blood product transfusion reactions to the laboratory and, as appropriate, to Federal and State authorities.

Interpretive Guidelines §493.1103(d)

Review the procedures for preventing, identifying, and investigating transfusion reactions. Examine records of transfusion reaction investigations for completeness, promptness, and accuracy. Verify that investigations of transfusion reactions are conducted in accordance with the facility's established protocols. Also, verify that incidents such as incomplete compatibility testing or issuing the wrong unit to a specific patient are reported to the appropriate authorities. Records should include each step in the investigation and identify the reviewer.

For facilities that provide transfusion services, confirm that all transfusion reactions identified have been investigated and the Food and Drug Administration (FDA) has been notified. If FDA has not been notified, notify the FDA at:

Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
Director, Office of Compliance and Biologics Quality
Attn: Fatality Program Manager (HFM-650)
1401 Rockville Pike

Rockville, MD 20852-1448
Voicemail: 301-827-6220
E-mail: fatalities2@cber.fda.gov
Fax: 301-827-6748

NOTE: Send the RO reports of all the fatal transfusion reactions identified. These reports are used to ensure that the facilities have properly notified FDA of fatal transfusion reactions and that both CMS and FDA have conducted all necessary follow-ups.

Probes §493.1103(d)

Are problems detected during the course of the transfusion reaction investigation documented, and are procedures instituted to prevent a recurrence?

§493.1105 Standard: Retention requirements.

(a) The laboratory must retain its records and, as applicable, slides, blocks, and tissues as follows:

Interpretive Guideline §493.1105(a)

The regulation applies to manual as well as automated record system, i.e., laboratory information system (LIS). However, the regulation does not specify the mechanism or frequency for which a laboratory should evaluate its record storage and retrieval system(s). The laboratory should establish its own policies and procedures for evaluating its system(s) and maintain documentation of the evaluation.

D3027

(a)(1) Test requisitions and authorizations. Retain records of test requisitions and test authorizations, including the patient's chart or medical record if used as the test requisition or authorization, for at least 2 years.

D3029

§493.1105 Standard: Retention requirements.

(a)(2) Test procedures. Retain a copy of each test procedure for at least 2 years after a procedure has been discontinued. Each test procedure must include the dates of initial use and discontinuance.

D3031

§493.1105 Standard: Retention requirements.

(a)(3) Analytic systems records. Retain quality control and patient test records (including instrument printouts, if applicable) and activities specified in §§493.1252 through 493.1289 for at least 2 years. In addition, retain the following:

Interpretive Guidelines §493.1105(a)(3)

The records must include instrument charts, graphs, printouts, transcribed data, and manufacturers' assay information sheets for control and calibration materials. If data is transcribed, ensure that the original and the transcribed copy are retained for 2 years.

Printouts from an instrument that is not directly interfaced with the laboratory information system must be retained for 2 years.

NOTE: Thermal paper or pressure sensitive paper may fade over time. The laboratory must copy applicable result printouts.

The laboratory is responsible for retaining records of interpretive slide results of each gynecologic and nongynecologic cytology case that each cytotechnologist examined or reviewed for at least five years.

D3033

§493.1105 Standard: Retention requirements.

(a)(3)(i) Records of test system performance specifications that the laboratory establishes or verifies under §493.1253 for the period of time the laboratory uses the test system but no less than 2 years.

D3035

§493.1105 Standard: Retention requirements.

(a)(3)(ii) Immunohematology records, blood and blood product records, and transfusion records as specified in 21 CFR 606.160(b)(3)(ii), (b)(3)(iv), (b)(3)(v), and (d).

Interpretive Guidelines §493.1105(a)(3)(ii)

Refer to the current version of 21 CFR Parts 600-799 for the specified section.

Non-transfusion related immunohematology patient testing and quality control (QC) records, such as instrument function checks, maintenance, and temperature records, must be retained for at least 2 years.

Other immunohematology patient and QC records related to transfusion testing, including but not limited to, donor processing, compatibility testing, and transfusion reaction investigations, must be retained for the time frame stated at 21 CFR 606.160(d). This also includes the visual inspection of whole blood and red blood cells during storage and immediately before distribution [21CFR 606.160(b)(3)(ii)], record of reissue, including records of proper temperature maintenance [21CFR 606.160(b)(3)(iv)], and emergency release of blood, including signature of requesting physician obtained before or after release [21CFR 606.160(b)(3)(v)].

D3037

§493.1105 Standard: Retention requirements.

(a)(4) Proficiency testing records. Retain all proficiency testing records for at least 2 years.

Interpretive Guidelines §493.1105(a)(4)

Proficiency testing (PT) records include all information regarding the PT event including testing records, signed attestation statements sent or transmitted to the PT providers, PT

results and scores from the provider, documentation of review and records of any corrective actions.

D3039

§493.1105 Standard: Retention requirements.

(a)(5) Laboratory quality system assessment records. Retain all laboratory quality system assessment records for at least 2 years.

Interpretive Guidelines §493.1105(a)(5)

Quality assessment (QA) records do not need to be maintained and stored in one location. The records may be stored in the specific area or department appropriate to the monitoring and evaluation of the laboratory activities (preanalytic, analytic, and postanalytic).

D3041

§493.1105 Standard: Retention requirements.

(a)(6) Test reports. Retain or be able to retrieve a copy of the original report (including final, preliminary, and corrected reports) at least 2 years after the date of reporting. In addition, retain the following:

Interpretive Guidelines §493.1105(a)(6)

The patient's chart or medical record may be used to report test results in lieu of a separate reporting form.

A copy of the original report includes all information sent to the individual requesting the test or using the test result(s), and includes the name and address of the laboratory performing the test. The copy need not be paper, but may be retrieved from a computer system, microfilm or microfiche record, as long as it contains the exact information in the same format as sent to the individual ordering the test or utilizing the test results. For tests requiring an authorized signature or containing personnel identifiers, the copy must include the signatures or identifiers (e.g., Pathology reports). "Pathology" includes all of its subspecialties (i.e., Histopathology, Oral pathology, Cytology).

A "preliminary report" means a test result that has been reported to the authorized person or laboratory that initially requested the test before the final test result is completed. Frequently, a preliminary report will contain significant, but not definitive information (e.g., a urine culture preliminary report of >100,000 Gram-negative bacilli after 24 hours incubation or a beta subunit preliminary report of >200 miu/ml). It should be noted on the report when the result is a preliminary result and that a final report will follow.

A "partial report" means multiple tests are ordered on the same specimen or patient. If partial reports are issued for only those tests that have been completed, then the report date will be the date when all tests have been completed. However, the laboratory should be able to identify the date that each new test is appended to the report.

The laboratory must have a system for retaining copies of all reports including original, preliminary, corrected, and final reports. This includes computer-generated reports.

Probes §493.1105(a)(6)

How has the laboratory verified that its record retrieval system functions appropriately?

(a)(6)(i) Immunohematology reports as specified in 21 CFR 606.160(d).

Interpretive Guidelines §493.1105(a)(6)(i)

Refer to the current version of 21 CFR Parts 600-799 for the specified section.

All Immunohematology test reports that are not transfusion-related must be retained for at least 2 years.

Transfusion-related Immunohematology test reports, including but not limited to, donor processing [§493.1271(b)], compatibility testing, and transfusion reaction investigations, must be retained for the time frame stated at 21 CFR 606.160(d).

(a)(6)(ii) Pathology test reports for at least 10 years after the date of reporting.

D3043

§493.1105 Standard: Retention requirements.

(a)(7) Slide, block, and tissue retention--

(a)(7)(i) Slides.

(a)(7)(i)(A) Retain cytology slide preparations for at least 5 years from the date of examination (see §493.1274(f) for proficiency testing exception).

Interpretive Guidelines §493.1105(a)(7)(i)(A)

For storage and maintenance requirements use D3013.

NOTE: *Cytology specimens include fine needle aspirates.*

Retention of cytology slides:

A laboratory refers all cytology specimens to a reference laboratory for examination. The reference laboratory examines all slide preparations and reports results only on normal, negative, and unsatisfactory cases. At the request of the referring laboratory, the reference laboratory returns those cases that have reactive, reparative atypia (including repair), LSIL, HSIL, all invasive squamous carcinomas, adenocarcinoma, all other malignant neoplasms, and 10% of the normal or negatives cases (including reactive and reparative cases) for quality control review. The referring laboratory must maintain the slides of the cases that it examines and for which it provides diagnosis (i.e., slides exhibiting atypical including repair, LSIL, HSIL, all invasive squamous carcinomas, adenocarcinoma, all other malignant neoplasms, and slides chosen for the 10% rescreen).

The laboratory must maintain documentation to acknowledge the donation of each slide submitted to a proficiency testing program or loaned for other purposes.

Probes §493.1105(a)(7)(i)(A)

What protocol has been established to ensure prompt return of slides, when necessary?

(a)(7)(i)(B) Retain histopathology slides for at least 10 years from the date of examination.

(a)(7)(ii) Blocks. Retain pathology specimen blocks for at least 2 years from the date of examination.

(a)(7)(iii) Tissue. Preserve remnants of tissue for pathology examination until a diagnosis is made on the specimen.

D3045

§493.1105 Standard: Retention requirements.

(b) If the laboratory ceases operation, the laboratory must make provisions to ensure that all records and, as applicable, slides, blocks, and tissue are maintained and available for the time frames specified in this section.

D8100

(Rev. 32, 02-13-2004)

Subpart Q--Inspection

§493.1771 Condition: Inspection requirements applicable to all CLIA-certified and CLIA-exempt laboratories.

(a) Each laboratory issued a CLIA certificate must meet the requirements in §493.1773 and the specific requirements for its certificate type, as specified in §§493.1775 through 493.1780.

(b) All CLIA-exempt laboratories must comply with the inspection requirements in §§493.1773 and 493.1780, when applicable.

D8101

§493.1773 Standard: Basic inspection requirements for all laboratories issued a CLIA certificate and CLIA-exempt laboratories.

(a) A laboratory issued a certificate must permit CMS or a CMS agent to conduct an inspection to assess the laboratory's compliance with the requirements of this part. A CLIA-exempt laboratory and a laboratory that requests, or is issued a certificate of accreditation, must permit CMS or a CMS agent to conduct validation and complaint inspections.

Interpretative Guidelines §493.1773(a)

If for any reason a facility denies entry to or does not permit you to conduct a survey, the following steps should be taken:

- *Explain your authority to conduct the survey and the consequences of failure to permit a survey;*
- *If necessary, consult with your supervisor or the RO; and*
- *For failure to permit entry into or on inspection of the laboratory, use D8101.*

If the laboratory continues to refuse a survey, refer to Subpart R – Enforcement Procedures and the Adverse Action Procedures in the SOM.

Conduct complaint surveys on an unannounced basis. All other surveys should be announced. See the policy for announcing surveys in the SOM.

The CLIA application will solicit the laboratory's hours of operation. For complaint or revisit surveys, you may phone the laboratory to confirm the hours of testing prior to a survey without revealing your identity or the scheduled date.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible; accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, e.g., physician's offices, clinics, residential care facilities, hospitals, respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

Maintain documentation for all on-site follow-up surveys in the laboratory's official file.

D8103

§493.1773 Standard: Basic inspection requirements for all laboratories issued a CLIA

certificate and CLIA-exempt laboratories.

(b) General requirements. As part of the inspection process, CMS or a CMS agent may require the laboratory to do the following:

Interpretative Guidelines §493.1773(b)-(c)

The regulations do not require a laboratory to maintain records on-site. During the survey, the laboratory must be able to retrieve copies of all records and necessary information upon request. Determine what constitutes a reasonable timeframe based on the information requested.

- (b)(1) Test samples, including proficiency testing samples, or perform procedures.**
- (b)(2) Permit interviews of all personnel concerning the laboratory's compliance with the applicable requirements of this part.**
- (b)(3) Permit laboratory personnel to be observed performing all phases of the total testing process (preanalytic, analytic, and postanalytic).**
- (b)(4) Permit CMS or a CMS agent access to all areas encompassed under the certificate including, but not limited to, the following:**
 - (b)(4)(i) Specimen procurement and processing areas.**
 - (b)(4)(ii) Storage facilities for specimens, reagents, supplies, records, and reports.**
 - (b)(4)(iii) Testing and reporting areas.**
- (b)(5) Provide CMS or a CMS agent with copies or exact duplicates of all records and data it requires.**
- (c) Accessible records and data.** A laboratory must have all records and data accessible and retrievable within a reasonable time frame during the course of the inspection.
- (d) Requirement to provide information and data.** A laboratory must provide, upon request, all information and data needed by CMS or a CMS agent to make a determination of the laboratory's compliance with the applicable requirements of this part.

D8105

§493.1773 Standard: Basic inspection requirements for all laboratories issued a CLIA certificate and CLIA-exempt laboratories.

(e) Reinspection. CMS or a CMS agent may reinspect a laboratory at any time to evaluate the ability of the laboratory to provide accurate and reliable test results.

Interpretative Guidelines §493.1773(e)

If for any reason a facility denies entry to or does not permit you to conduct a survey, the following steps should be taken:

- *Explain your authority to conduct the reinspection and the consequences of failure to permit a survey;*
- *If necessary, consult with your supervisor or the RO; and*
- *For failure to permit entry into or on inspection of the laboratory, use D8101.*

If the laboratory continues to refuse a survey, refer to Subpart R – Enforcement Procedures and the Adverse Action Procedures in the SOM.

Conduct complaint surveys on an unannounced basis. All other surveys should be announced. See the policy for announcing surveys in the SOM.

The CLIA application will solicit the laboratory's hours of operation. For complaint or revisit surveys, you may phone the laboratory to confirm the hours of testing prior to a survey without revealing your identity or the scheduled date.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, e.g., physician's offices, clinics, residential care facilities, hospitals, respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

Maintain documentation for all on-site follow-up surveys in the laboratory's official file.

(f) Complaint inspection. CMS or a CMS agent may conduct an inspection when there are complaints alleging noncompliance with any of the requirements of this part.

Interpretative Guidelines §493.1773(f)

If for any reason a facility denies entry to or does not permit you to conduct a survey, the following steps should be taken:

- *Explain your authority to conduct the inspection and the consequences of failure to permit a survey;*
- *If necessary, consult with your supervisor or the RO; and*
- *For failure to permit entry into or on inspection of the laboratory, use D8101.*

If the laboratory continues to refuse a survey, refer to Subpart R – Enforcement Procedures and the Adverse Action Procedures in the SOM.

Conduct complaint surveys on an unannounced basis. All other surveys should be announced. See the policy for announcing surveys in the SOM.

The CLIA application will solicit the laboratory's hours of operation. For complaint or revisit surveys, you may phone the laboratory to confirm the hours of testing prior to a survey without revealing your identity or the scheduled date.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, e.g., physician's offices, clinics, residential care facilities, hospitals, respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

Maintain documentation for all on-site follow-up surveys in the laboratory's official file.

(g) Failure to permit an inspection or reinspection. Failure to permit CMS or a CMS agent to conduct an inspection or reinspection results in the suspension or cancellation of the laboratory's participation in Medicare and Medicaid for payment, and suspension or limitation of, or action to revoke the laboratory's CLIA certificate, in accordance with subpart R of this part.

Interpretative Guidelines §493.1773(g)

If for any reason a facility denies entry to or does not permit you to conduct a survey, the following steps should be taken:

- *Explain your authority to conduct the survey and the consequences of failure to permit a survey;*
- *If necessary, consult with your supervisor or the RO; and*
- *For failure to permit entry into or on inspection of the laboratory, use D8101.*

If the laboratory continues to refuse a survey, refer to Subpart R – Enforcement Procedures and the Adverse Action Procedures in the SOM.

Conduct complaint surveys on an unannounced basis. All other surveys should be announced. See the policy for announcing surveys in the SOM.

The CLIA application will solicit the laboratory's hours of operation. For complaint or revisit surveys, you may phone the laboratory to confirm the hours of testing prior to a survey without revealing your identity or the scheduled date.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, e.g., physician's offices, clinics, residential care facilities, hospitals, respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

Maintain documentation for all on-site follow-up surveys in the laboratory's official file.

§493.1775 Standard: Inspection of laboratories issued a certificate of waiver or a certificate for provider-performed microscopy procedures.

(a) A laboratory that has been issued a certificate of waiver or a certificate for provider-performed microscopy procedures is not subject to biennial inspections.

Interpretative Guidelines §493.1775(a)

To cite deficiencies related to an inspection of a laboratory holding a certificate of waiver or a certificate of provider performed microscopy procedures, use D8100, D8101 and D8103, as appropriate.

(b) If necessary, CMS or a CMS agent may conduct an inspection of a laboratory issued a certificate of waiver or a certificate for provider-performed microscopy procedures at any time during the laboratory's hours of operation to do the following:

Interpretative Guidelines §493.1775(b)

In any laboratory holding a CLIA certificate, tests listed on the waived list are not subject to routine surveys. A survey for waived tests may be conducted only when authorized by the RO in one of the following instances:

- To collect information on waived tests;
- To determine whether the laboratory is testing beyond its certificate;
- If a complaint is alleged; or
- You have information that the performance of such tests poses an imminent and serious risk that adversely affects patient test results.

When authorized to perform a survey of waived tests, in addition to the requirements in this subpart, refer to the requirements at §493.15, subpart A, and §§493.35, 493.37 and 493.39, subpart B, of these guidelines.

Section 493.35(d) requires that laboratories performing only waived tests and no other tests must agree to permit inspections by HHS in order to receive a certificate of waiver.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, (i.e., physician's offices, clinics, residential care facilities, hospitals, etc.), respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

- (b)(1) Determine if the laboratory is operated and testing is performed in a manner that does not constitute an imminent and serious risk to public health.
- (b)(2) Evaluate a complaint from the public.
- (b)(3) Determine whether the laboratory is performing tests beyond the scope of the certificate held by the laboratory.

Interpretative Guidelines §493.1775(b)(3)

When a laboratory has failed to obtain a registration certificate before performing and reporting patient results for non-waived testing, notify the RO of a possible action by the Office of the Inspector General (OIG) if the laboratory does not obtain the appropriate certificate or cease the non-waived testing.

- (b)(4) Collect information regarding the appropriateness of tests specified as waived tests or provider-performed microscopy procedures.
- (c) The laboratory must comply with the basic inspection requirements of §493.1773.

§493.1777 Standard: Inspection of laboratories that have requested or have been issued a certificate of compliance.

(a) Initial inspection.

Interpretative Guidelines §493.1777(a)

If for any reason a facility denies entry to or does not permit you to conduct a survey, take the following steps:

- *Explain your authority to conduct the survey and the consequences of failure to permit a survey;*
- *If necessary, consult with your supervisor or the RO; and*
- *For failure to permit entry into or an inspection of the laboratory, use D8101.*

If the laboratory continues to refuse a survey refer to Subpart R – Enforcement Procedures and the Adverse Action procedures beginning at §493.6300 of the SOM.

(a)(1) A laboratory issued a registration certificate must permit an initial inspection to assess the laboratory's compliance with the requirements of this part before CMS issues a certificate of compliance.

(a)(2) The inspection may occur at any time during the laboratory's hours of operation.

(b) Subsequent inspections.

(b)(1) CMS or a CMS agent may conduct subsequent inspections on a biennial basis or with such other frequency as CMS determines to be necessary to ensure compliance with the requirements of this part.

(b)(2) CMS bases the nature of subsequent inspections on the laboratory's compliance history.

Interpretative Guidelines §493.1777(b)

In any laboratory holding a CLIA certificate, tests listed on the waived list are not subject to routine surveys. A survey for waived tests may be conducted only when authorized by the RO in one of the following instances:

- *To collect information on waived tests;*
- *To determine whether the laboratory is testing beyond its certificate;*
- *If a complaint is alleged; or*
- *You have information that the performance of such tests poses an imminent and serious risk that adversely affects patient test results.*

When authorized to perform a survey of waived tests, in addition to the requirements in

this subpart, refer to the requirements at §493.15, subpart A, and §§493.35, 493.37 and 493.39, subpart B, of these guidelines.

Section 493.35(d) requires that laboratories performing only waived tests and no other tests must agree to permit inspections by HHS in order to receive a certificate of waiver.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as much as possible. In facilities providing direct patient care, (i.e., physician's offices, clinics, residential care facilities, hospitals, etc.), respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

(c) Provider-performed microscopy procedures. The inspection sample for review may include testing in the subcategory of provider-performed microscopy procedures.

(d) Compliance with basic inspection requirements. The laboratory must comply with the basic inspection requirements of Sec. 493.1773.

D8401

§493.1780 Standard: Inspection of CLIA-exempt laboratories or laboratories requesting or issued a certificate of accreditation.

(a) Validation inspection. CMS or a CMS agent may conduct a validation inspection of any accredited or CLIA-exempt laboratory at any time during its hours of operation.

Interpretative Guidelines §493.1780

Validation surveys of accredited laboratories will be conducted by the State survey agencies. Refer to special procedures for accredited laboratories in the SOM. The RO is responsible for conducting validations of CLIA-exempt laboratories.

(b) Complaint inspection. CMS or a CMS agent may conduct a complaint inspection of a CLIA-exempt laboratory or a laboratory requesting or issued a certificate of accreditation at any time during its hours of operation upon receiving a complaint applicable to the requirements of this part.

Interpretative Guidelines §493.1780(b)

In any laboratory holding a CLIA certificate, tests listed on the waived list are not subject to routine surveys. A survey for waived tests may be conducted only when authorized by the RO in one of the following instances:

- To collect information on waived tests;
- To determine whether the laboratory is testing beyond its certificate;
- If a complaint is alleged; or
- You have information that the performance of such tests poses an imminent and serious risk that adversely affects patient test results.

When authorized to perform a survey of waived tests, in addition to the requirements in this subpart, refer to the requirements at §493.15, subpart A, and §§493.35, 493.37 and 493.39, subpart B, of these guidelines.

Section 493.35(d) requires that laboratories performing only waived tests and no other tests must agree to permit inspections by HHS in order to receive a certificate of waiver.

Make every effort to minimize the impact of the survey on the laboratory operations and patient care activities. Be flexible, accommodate staffing schedules and workloads as

much as possible. In facilities providing direct patient care, (i.e., physician's offices, clinics, residential care facilities, hospitals, etc.), respect patient privacy and do not interrupt or interfere with patient care. Be well prepared, courteous and make requests, not demands.

(c) *Noncompliance determination.* If a validation or complaint inspection results in a finding that the laboratory is not in compliance with one or more condition-level requirements, the following actions occur:

(c)(1) A laboratory issued a certificate of accreditation is subject to a full review by CMS, in accordance with subpart E of this part and §488.11 of this chapter.

(c)(2) A CLIA-exempt laboratory is subject to appropriate enforcement actions under the approved State licensure program.

(d) *Compliance with basic inspection requirements.* CLIA-exempt laboratories and laboratories requesting or issued a certificate of accreditation must comply with the basic inspection requirements in §493.1773.