Flow Cytometry

CLIA Compliance Manual*

Revised for the

International Society for Advancement of Cytometry (ISAC)
and
Clinical Cytometry Society (CCS)

By

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^ "1st Edition
The first edition of this manual was commissioned for the Purdue CDROM
Vol 3, 1997 and was written by A. Hurley and D. Zito.

Preface

The 105th Congress of the United States, convened after the January 1997 inauguration of President Clinton, considered many issues affecting clinical laboratory science in general and cytometry laboratories in particular. Conformation to the provisions of the Clinical Laboratory Improvement Act (CLIA), Medicare fee schedule changes, manpower funding, and reimbursement issues all came under Congressional scrutiny. After a series of revisions, the CLIA Final Rule (42 CFR Part 493 (68 FR:3640) was published in January 2003 and implemented April 24, 2003. Minor changes were incorporated in 2004. There are changes relating to Quality Systems and Personnel Requirements. In addition, there are consolidations around requirements for patient test management and changes in grading for proficiency testing.

Because of this fluid regulatory environment, the Flow Cytometry CLIA Compliance Manual has been written to help make sense of the CLIA requirements and give laboratories a clear format by which to monitor Quality Assessment (previously Quality Assurance) and Quality Control. This manual outlines the updated compliance requirements for clinical laboratories engaged in the practice of flow cytometry, which is now considered non-waived testing (previously high complexity). Only the personnel requirements continue to stratify the "high complexity" and "moderate complexity" categorization. In recent years, the complexity of flow cytometry assays has increased significantly, particularly in relation to the number of simultaneous measurements that can now be made. Areas of spectral overlap, accuracy of data collection, cluster identification automation, and approaching issues of complex data processing can cause many problems if not addressed appropriately. Since the legislative requirements are based on the complexity of the laboratory testing, recommendations in this manual apply to non-waived testing; instructions and forms are provided for complying with the personnel, quality control, proficiency testing, and quality assessment requirements.

ISAC and CCS play an important role in all aspects of laboratory management, establishment of standards as well as training and education for the field of cytometry. There is no substitute for well documented processes, assays and results reporting. All documents of this nature are living documents and we encourage you to participate in the identification of areas that can be updated or modified to improve clarity, accuracy or relevance. The ISAC Education Task Force in conjunction with CCS has developed an updated version of this manual to incorporate the final CLIA revisions. We hope the information put forth here will help cytometry laboratories meet these regulatory requirements with greater ease, so that they may focus with more intensity on the quality of patients' results.

While every effort has been made to ensure the accuracy of this document, the 2004 Codification is the definitive document. The current link to this document is: http://www.access.gpo.gov/nara/cfr/waisidx_04/42cfr493_04.html.

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Introduction

This manual will outline key areas for clinical laboratories engaged in the practice of flow cytometry abstracted from the Final Rule of the Clinical Laboratory Improvement Act (CLIA) compliance requirements through 2004. The legislation requirements are based on the complexity of the laboratory testing. Flow cytometry is considered high complexity testing; however, the revised CLIA document combines the moderate and high complexity testing in to one category; “non-waived” tests. The only area where “high complexity” testing is singled out is in the Personnel area. The recommendations in this manual will apply to non-waived testing and will give information and example forms for complying with the personnel, quality control, proficiency testing, and quality assessment requirements.

Subpart H

Participation in Proficiency Testing (PT) for Laboratories Performing Non-waived Tests

493.801 Condition: Enrollment and Testing of Samples

Each laboratory performing non-waived tests must enroll in a proficiency testing program that meets the CLIA federal regulation (Subpart I) and is approved by Health and Human Services (HHS). The laboratory must enroll in an approved program or programs for each of the specialties or subspecialties for which certification is desired. All of the usual criteria for running proficiency testing samples must be adhered to, including running each test sample as a patient.

Under the regulation (a) **Standard; Enrollment**, the laboratory is required to:

Inform HHS of the approved programs in which it has chosen to participate. The laboratory must also list the tests performed and which PT programs will satisfy this requirement. For tests that are not covered under PT programs, the laboratory must establish and maintain the accuracy and reliability of its testing procedures in accordance with section 493.1236 The laboratory must also participate in the approved program or programs for one year for each specialty or test before choosing a different program and must notify CMS before the change. The last requirement under this Standard asks the laboratory to authorize the PT program to release to HHS all data necessary to determine the laboratory's compliance.

Under the regulation (b) **Standard; Testing of Proficiency Testing Samples**, the laboratory is required to:

Test or examine the PT samples it receives with the regular patient workload by personnel who routinely perform the testing using the usual methods. The laboratory must handle and test PT samples the same number of times it routinely tests patient samples. Additionally, the laboratory must not discuss PT sample results with any other laboratory until after the results are required to be sent to the service. This also applies to laboratories with multiple sites. If a laboratory performs a certain test, it must not send the PT sample to another laboratory for analysis and then report those results. Laboratories who engage in this practice will have their certification revoked for at least one year.

The laboratory must follow standard practices by documenting the handling, preparation, processing, examination, and each step in the testing and reporting of results for all PT samples. Copies of the PT report forms (with the signatures of the analyst and laboratory director) must be kept for a minimum of two years after the PT event. Only the primary method for patient testing requires PT data.

493.803 Condition: Successful Participation

Each laboratory performing non-waived tests must successfully participate in a PT program approved by CMS, if applicable. If the laboratory fails the PT program for any specialty, subspecialty, analyte, or test, sanctions will be taken. The proficiency testing grading requirement is 80% consensus among participating laboratories.

493.807 Condition: Reinstatement of Laboratories Performing Non-waived Tests After Failure to Participate Successfully.

The termination period for Medicare/Medicaid approval or period for suspension of certification under CLIA for the failed test, is a period of not less than six months. If the laboratory's certificate is suspended or Medicare/Medicaid approval is withdrawn for failing PT for one or more tests, or if the laboratory voluntarily withdraws its certification, the laboratory must demonstrate successful performance on two consecutive PT events (one of which may be on-site) before CMS will consider it for reinstatement.

NOTE: Please refer to the CLIA regulation, **Proficiency Testing by Specialty or Subspecialty for Laboratories Performing Non-waived Tests** for the specific parameters required for successful PT performance.

Subpart I

Proficiency Testing Programs for Non-waived Tests

493.901 Approval of proficiency testing programs

A PT program must be offered by a private, nonprofit organization, a Federal or State agency or its designee in order to receive HHS approval. The organization must submit its application for approval or re-approval for the next calendar year by July 1 of the current year. It must also provide technical assistance to laboratories which desire to qualify under the program. Additionally, the organization must assure the quality of test samples, evaluate and score the results, and identify performance deficits. Overall technical ability must be demonstrated to HHS. This includes: the preparation or purchase of samples made under good manufacturing practices; the adequate distribution of samples, with special consideration given to patient similarity, homogeneity, and stability; and mechanisms to provide adequate information to HHS and the PT participant on grading criteria, technical and administrative concerns.

493.903 Administrative responsibilities.

The proficiency testing program must provide HHS or its designees and participating laboratories with an electronic or a hard copy, or both, of reports of proficiency testing results and all scores for each laboratory's performance within 60 days after the date by which the laboratory must report proficiency testing results to the proficiency testing program.

The program also must furnish to HHS cumulative reports on an individual laboratory's performance and aggregate data for the purpose of establishing a system to make the proficiency testing program's results available, on a reasonable basis, upon request of any person, and include such explanatory information as may be appropriate to assist in the interpretation of the proficiency testing program's results.

The program must provide HHS with an annual report and, if needed, an interim report which identifies any previously unrecognized sources of variability in kits, instruments, methods, or PT samples, which adversely affect the programs' ability to evaluate laboratory performance.

493.905 Non-approved proficiency testing programs.

If a proficiency testing program is determined by HHS to fail to meet any criteria contained in Secs. 493.901 through 493.959 for approval of the proficiency testing program, CMS will notify the program and the program must notify all laboratories enrolled of the non-approval and the reasons for non-approval within 30 days of the notification.

Subpart J
Facility Administration
for Non-waived testing

493.1101 Standard; Facilities

The laboratory must be constructed to ensure an appropriate environment to enable the proper performance of all phases of testing (pre-analytic, analytic, and post-analytic). Safety precautions must be followed to ensure protection from biohazardous materials, and from electrical or physical hazards.

493.1105 Standard: Retention requirements

The laboratory must retain its records and, as applicable, slides, blocks, and tissues as follows:

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.

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.

Analytic systems records. Retain quality control and patient test records (including instrument printouts, if applicable) and all analytic systems activities specified in through for at least 2 years*. In addition, retain records of test system performance specifications that the laboratory establishes or verifies for the period of time the laboratory uses the test system but no less than 2 years.

Proficiency testing records. Retain all proficiency testing records for at least 2 years.

Laboratory quality systems assessment records. Retain all laboratory quality systems assessment records for at least 2 years.

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.

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.

***Note**: Flow cytometry dot plots and gated histograms must be stored for 10 years (CAP) . Electronic listmode files are acceptable, providing the analysis gates used to derive the results are imbedded within the file.

Subpart K

Quality Systems for Non-waived Testing

The section has been revised in 2003 to incorporate quality assessment (previously quality assurance), quality control, and general laboratory systems, which include pre-analytic, analytic and post analytic processes. It also combines moderate complexity and high complexity testing into non-waived tests

493.1200 Introduction

(a) Each laboratory that performs non-waived testing must establish and maintain written policies and procedures that implement and monitor quality systems for all phases of the total testing process (that is, pre-analytic, analytic, and post-analytic) as well as general laboratory systems.

(b) Each of the laboratory's quality systems must include an 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 components of the laboratory's quality systems 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.

General Laboratory Systems

493.1230 Condition: General laboratory systems

Each laboratory that performs non-waived testing must meet the applicable general laboratory systems requirements in Sec. 493.1231 through 493.1236, 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 general laboratory systems and correct identified problems as specified in Sec. 493.1239 for each specialty and subspecialty of testing performed.

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.

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.

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.

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 individual who orders or receives test results.

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.

493.1236 Standard: Evaluation of proficiency testing performance

The laboratory must review and evaluate the results obtained on proficiency testing performed as specified in subpart H of this part. The laboratory must verify the accuracy of the following: 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 or 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 of results).

At least twice annually, the laboratory must verify the accuracy of the following: any test or procedure it performs that is not included in subpart I of this part, or 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. All proficiency testing evaluation and verification activities must be documented.

493.1239 Standard: General laboratory systems assessment

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 system requirements specified at Sec. Sec. 493.1231 through 493.1236.

The general laboratory 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 general laboratory systems assessment reviews with appropriate staff.

The laboratory must document all general laboratory systems assessment activities.

Pre-analytic Systems

493.1240 Condition: Pre-analytic systems

Each laboratory that performs non-waived testing must meet the applicable pre-analytic system(s) requirements in Sec. Sec. 493.1241 and 493.1242, 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 pre-analytic systems and correct identified problems as specified in Sec. 493.1249 for each specialty and subspecialty of testing performed.

493.1241 Standard; Test Requisition

Tests are performed by a laboratory only at the written or electronic request of an authorized person. Verbal requests must be followed by written or electronic authorization within 30 days. The test requisitions (or equivalent) must be retained for a minimum of two years. Each requisition must include: a unique patient identifier, any suitable identifiers of the requesting party, the tests to be performed, and the date and time of specimen collection.

493.1242, Standard; Procedures for Specimen Submission and Handling

Each laboratory must have written policies and procedures (readily available) for all methods. These include: preparation of patients, specimen collection, specimen labeling, specimen preservation, and specimen transportation. If the laboratory accepts referral specimens, the above information must be supplied to their clients.

493.1249 Standard: Pre-analytic systems assessment

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 pre-analytic systems. The pre-analytic 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 pre-analytic systems assessment reviews with appropriate staff. The laboratory must document all pre-analytic systems assessment activities.

Analytic Systems

493.1250 Condition: Analytic systems

Each laboratory that performs nonwaived testing must meet the applicable analytic systems requirements. The laboratory must monitor and evaluate the overall quality of the analytic systems and correct identified problems.

493.1251 Standard: Procedure manual

A written procedure manual for the performance of all analytical methods used by the laboratory must be readily available and followed by laboratory personnel. Procedures may be organized in the form of manuals, computer memory, or card files. Manufacturer's operating instructions, package inserts, and other manuals (CDC or AFIP) are acceptable as long as the procedures are clearly indicated. The procedure manual must include: requirements for specimen collection, processing and specimen rejection criteria, step-by-step performance of the procedure, preparation of solutions, calibrators, controls and reagents, calibration and calibration verification procedures, the reportable range for test results, and control procedures. The procedure manual must also include the remedial action required when calibration or control results fall outside the laboratory's acceptability criteria. Defined reference ranges, "panic values", literature references, criteria for specimen storage and the laboratory's system for reporting patient results must be clearly documented and available to all laboratory personnel. Procedures must be approved, signed, and dated by the director prior to implementation and must be reapproved if the director changes. The laboratory must maintain a copy of each procedure in a secure location with the date of the initial use and discontinuance for a minimum of 2 years after a procedure has been discontinued.

493.1252 Standard: Test systems, equipment, instruments, reagents, materials, and supplies

Accurate and reliable results must be obtained by ensuring that the equipment and methodologies are performed within the laboratory's stated performance specifications. A laboratory must define criteria for conditions essential for proper storage of reagents, specimens and accurate and reliable test system operation and test result reporting. Such conditions may include: water quality, temperature, humidity and electrical current fluctuation protection. Any remedial actions must be documented. Reagents, solutions, culture media, control materials, calibration materials and other supplies must be labeled for: identity and titer or concentration, recommended storage requirements, preparation and expiration dates. The laboratory must comply with FDA product dating requirements and not use materials when they have exceeded their expiration date. Additionally, the laboratory must not interchange components of reagent kits of different lot numbers unless so specified by the manufacturer.

493.1253 Standard: Establishment and verification of performance specifications

Before a laboratory can report patient results, it must verify or establish performance specifications for accuracy, precision, sensitivity and specificity (if applicable), the reportable

range of patient test results, the normal values, and any other applicable performance characteristics. Laboratories are required to verify or establish performance criteria for a test method in use after April 23, 2003. Laboratories are not required to verify or establish performance specifications for any test system used by the laboratory before April 24, 2003

The laboratory must determine and establish the test systems calibration and control procedures for monitoring and evaluating the quality of the analytical testing process of each method to assure the accuracy and reliability of patient test results and reports. The responsibility for quality now rests on the laboratory as there is no longer FDA clearance of QC. The laboratory is responsible for having control procedures that monitor the complete analytical process, take into account the performance specifications of the method, detect immediate errors, and monitor long term precision and accuracy.

For each non-waived test, the laboratory must meet all applicable standards of this subpart. For each non-waived test performed using a method developed in-house or using an instrument, kit or test system cleared by the FDA through the premarket notification (510(k)) or premarket approval (PMA) process but modified by the laboratory, the laboratory must meet all applicable standards of this subpart. However, for all other non-waived tests performed using an instrument, kit or test system cleared by the FDA for in-vitro diagnostic use the laboratory must:

1. Follow the manufacturer's instructions for instrument or test system operation and test performance
2. Have a written procedure manual describing the processes for testing and reporting patient test results
3. Perform and document calibration and calibration verification procedures at least once every six months

4. Perform and document quality control procedures using at least two levels of control materials each day of testing
5. Perform and document applicable specialty and subspecialty control procedures as specified under 493.1223
6. Perform and document that remedial action has been taken when problems or errors are identified as specified in 493.1219

Electronic, mechanical, and operational checks must be performed by the laboratory to ensure proper performance and accurate test results. For equipment cleared by the FDA, the laboratory must perform and document the maintenance as defined by the manufacturer with at least the frequency specified. For equipment not cleared by the FDA or for equipment, instruments, or systems developed or modified in-house, the laboratory must establish and document a maintenance protocol which includes frequency of testing. In like manner, for equipment cleared by the FDA the laboratory must perform function checks as defined and with at least the frequency recommended. For equipment not cleared, or in-house modified or developed systems, the laboratory must define and document a function check protocol.

493.1255 Standard; Calibration and Calibration Verification Procedures

Calibration is the process of testing and adjusting an instrument or test system to provide a known relationship between the measurement response and the value of the substance that is being measured by the test procedure. Calibration verification is the assaying of calibration materials in the same manner as patient samples to confirm that the calibration of the instrument or test system has remained stable throughout the laboratory's reportable range for test results. Calibration and calibration verification must be performed and documented. For test procedures that are performed on test systems that have been cleared by the FDA, the laboratory must follow the manufacturer's directions at a minimum. For procedures developed or modified in-house, or systems not cleared by the FDA the laboratory must establish calibration procedures in accordance with criteria established by the laboratory. This criterion should include: the number, type and concentration of calibration materials, acceptable limits for calibration, frequency of calibration, and the appropriate calibration materials that are traceable to a reference method or reference material, if possible. Additionally, calibration must be performed when calibration verification fails to meet the laboratory's acceptable limits.

Calibration verification procedures must be performed with the manufacturer's instructions, or in accordance with criteria established by the laboratory. The calibration materials must be appropriate for verifying the laboratory's established reportable range of patient results which must include at least a minimal (or zero) value, a mid-point value, and a maximum value at the upper limit of that range. Calibration verification must also be performed at least once every six months or when a complete change of reagents for a procedure is introduced (unless the laboratory can demonstrate that the change does not affect the reportable range), when major preventive maintenance requires the replacement of critical parts that may influence test performance, and when the controls demonstrate an unusual trend or shift. All calibration and calibration verification procedures that are performed must be documented.

493.1256 Standard; Control Procedures

The accuracy and precision of patient test results are indirectly assessed through use of control procedures and control and calibration materials. For each method cleared by the FDA, the laboratory must follow the manufacturer's instructions. For methods developed or modified in-house, or not cleared by the FDA, the laboratory must evaluate instrument and reagent stability and operator variance in determining the number, type and frequency of testing calibration and control materials and establish acceptability criteria used to monitor test performance during a patient specimens run. (A run is an interval within which accuracy and precision of a testing system is expected to be stable, but cannot be greater than 24 hours.)

For qualitative tests, the laboratory must include a positive and negative control with each run of patient specimens. This can be commercial, previously tested samples or internal controls. For quantitative tests, the laboratory must include at least two samples of different concentrations of either calibration materials, control materials, or a combination, with a frequency of not less than once each run of patient specimens. The laboratory must have an alternative mechanism to assure the validity of patient results if calibration and control materials are not available. Control samples must be tested in the same manner as patient samples and results must meet the laboratory's acceptability criteria. When calibration or control materials are used, statistical values such as mean and standard deviation must be determined through repetitive testing. The manufacturer's stated values of an assayed control may be used, or, if unassayed materials are used, the laboratory must establish these values through concurrent testing with previously determined values of calibration or control materials.

493.1281 Standard: Comparison of test results

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. The laboratory must have a system to identify and assess patient test results that appear inconsistent with the following relevant criteria, when available: Patient age, sex, .diagnosis or pertinent clinical data, and relationship with other test parameters. The laboratory must document all test result comparison activities.

493.1282 Standard: Corrective actions

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. The laboratory must document all corrective actions taken, including actions taken when any of the following occur: test systems do not meet the laboratory's verified or established performance specifications., which include but are not limited to--equipment or methodologies that perform outside of established operating parameters or performance specifications; patient test values that are outside of the laboratory's reportable range of test results for the test system; and when the laboratory determines that the reference intervals for a test procedure are inappropriate for the laboratory's patient population,

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.

493.1283 Standard; Test Records

A record system must be maintained by the laboratory to ensure reliable identification of patient specimens (and the testing personnel) as they are processed and tested. Records, including instrument printouts if applicable, must be retained for a minimum of two years. These records must include: a unique patient identifier, the date and time the specimen arrived at the laboratory, the disposition of specimens that do not meet the laboratory's acceptability criteria, and the dates of all specimen testing. Laboratories are now required to retain flow cytometry dot plots and histograms for 10 years. (College of American Pathologists).Electronic listmode files are acceptable, providing the analysis gates used to derive the results are embedded within the file.

493.1289 Standard: Analytic systems assessment

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. The analytic 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 analytic systems assessment reviews with appropriate staff. The laboratory must document all analytic systems assessment activities.

Post Analytical Systems

493.1290 Condition: Post-analytic systems

Each laboratory that performs non-waived testing must meet the applicable post-analytic systems requirements. The laboratory must monitor and evaluate the overall quality of the post-analytic systems and correct identified problems for each specialty and subspecialty of testing performed.

493.1291 Standard; Test Report

The laboratory report must be sent promptly to the requesting individual or party. A copy of each report must be maintained by the laboratory for timely accessibility and for a minimum of two years. The test report must indicate the name and address of the laboratory location, the test performed, the test result, date of test report and, if applicable, specimen source, interpretation and/or the units of measurement. Pertinent reference or normal ranges, determined by the laboratory performing the tests, must be available to the requester. Additionally, the laboratory must develop and follow written procedures for reporting imminent life-threatening test results or panic values. If requested by its clients, the laboratory must provide a list of test methods employed and the performance specifications.

493.1299 Standard: Post-analytic systems assessment

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 post-analytic systems. The post-analytic 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 post-analytic systems assessment reviews with appropriate staff. The laboratory must document all post-analytic systems assessment activities.

Subpart M

Personnel for Non-waived Testing

NOTE: Personnel requirements are the only area where there is delineation between high and moderate complexity testing. This is based on a weighted system that reviews the following attributes of the testing: knowledge, training and experience, characteristics of the operational steps, calibration, QC, and PT materials, troubleshooting and maintenance, interpretation and judgment. Flow cytometry testing is classified as high complexity testing. This revision is effective as of February 24, 2003.

493.1401 General

This subpart consists of the personnel requirements that must be met by laboratories performing non-waived testing.

493.1441 Condition: Laboratories Performing Non-waived, (High Complexity Testing); Laboratory Director

The laboratory must have a director who meets the qualification requirements and provides overall management and direction.

493.1443 Standard; Laboratory Director Qualifications

The laboratory director must possess a current license as a director issued in the state in which the laboratory is located, if such is required. The director may be a doctor of medicine or osteopathy licensed to practice in that state and be certified in anatomic or clinical pathology or both or possess qualifications that are equivalent to those required for such certification. The director may also be a doctor of medicine or osteopathy duly licensed and have at least one year of laboratory training during residency or at least 2 years experience directing high complexity testing. The director may also hold an earned doctoral degree in a chemical, physical, biological, or clinical laboratory science from an accredited institution and be appropriately certified by a board approved by the HHS. Alternative qualifications include 2 years of laboratory training and 2 years laboratory experience directing or supervising high complexity prior to February 24, 2003.

493.1445 Standard; Laboratory Director Responsibilities

The laboratory director is responsible for the overall operation of the laboratory including employing acceptable personnel. The director may perform the duties of the technical consultant, clinical consultant, and testing personnel or delegate these to the appropriate personnel. The director must ensure that testing systems developed and used provide quality services that the physical plant conditions are appropriate for the testing performed, that the test methodologies

will provide quality results, that verification procedures are adequate, and that personnel are performing the tests as required. The director must also ensure that the laboratory is enrolled in an HHS approved PT program and that the QC and QA programs are established and maintained to assure quality and identify failures as they occur. Additionally, the director must ensure remedial action is taken when necessary, that consultation is available to the laboratory's clients, that sufficient laboratory personnel with the appropriate education and experience are performing the tests, that policies are established for monitoring personnel to assess their competency, that an approved procedure manual is available, and that the responsibilities of each person are specified. The director must also ensure that a general supervisor provides on-site supervision of non-waived test performance.

493.1447 Condition: Laboratories Performing Non-waived, (High Complexity Testing); Technical Supervisor

The laboratory must have a technical supervisor who meets qualification requirements and provides technical supervision.

493.1449 Standard; Technical Supervisor Qualifications (TS)

Individuals who are qualified by education and experience to provide technical supervision for the performed services must be employed by the laboratory. The TS must possess a current license issued in the state in which the laboratory is located, if such is required.

The TS may be a doctor of medicine or osteopathy licensed to practice in that state and be certified in anatomic or clinical pathology or both or possess qualifications that are equivalent to those required for such certification.

NOTE: Please refer to the CLIA regulation, for the applicable qualification requirements for the specific high complexity subspecialties for the technical supervisor.

493.1451 Standard; Technical Supervisor Responsibilities

The technical supervisor is responsible for the technical and scientific oversight of the laboratory. The TS is not required to be on-site at all times testing is performed, but must be available on an as-needed basis. The TS is responsible for the selection of the appropriate test methodology, ensuring that verification procedures are established. The TS must also ensure that the laboratory is enrolled in an HHS approved PT program and establish the QC and QA programs to assure quality and identify failures as they occur. Additionally, the TS must ensure remedial action is taken when necessary, resolve technical problems, ensure that each individual performing tests receives regular in-service training, and evaluate the competency of all testing personnel. Technical Supervisor Responsibilities: 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-

(i) Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing and testing;

(ii) Monitoring the recording and reporting of test results;

(iii) Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records;

(iv) Direct observation of performance of instrument maintenance and function checks;

(v) Assessment of test performance through testing previously analyzed specimens, internal blind testing samples or external proficiency testing samples; and

(vi) Assessment of problem solving skills.

Evaluating and documenting the performance of individuals responsible for high complexity testing at least semiannually during the first year the individual tests patient specimens. Thereafter, evaluations must be performed at least annually 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.

493.1453 Condition: Laboratories Performing Non-waived, (High Complexity Testing); Clinical Consultant

The laboratory must have a clinical consultant who meets the qualification requirements and provides clinical consultation.

493.1455 Standard; Clinical Consultant Qualifications (CC)

The CC must be qualified to consult with and render opinions to the laboratory's clients concerning the diagnosis, treatment and management of patient care. The CC must be qualified as a laboratory director, or be a doctor of medicine or osteopathy and possess a license to practice in the state in which the laboratory is located.

493.1457 Standard; Clinical Consultant Responsibilities

The CC provides consultation regarding the appropriateness of the tests ordered and the interpretation of results. This includes being available to the laboratory's clients to assist with choosing the appropriate tests and that the patient reports contain the pertinent information necessary for specific patient interpretation.

493.1459 Condition: Laboratories Performing Non-waived (High Complexity Testing); General Supervisor (GS)

The laboratory must have one or more general supervisors who are qualified to provide general supervision. The GS provides day-to-day supervision of testing personnel and reporting of test results under the direction of the laboratory director and the technical supervisor. The GS must possess a current license issued by the state where is laboratory is located, if required, be a laboratory director, or a technical supervisor.

NOTE: Please refer to the CLIA regulation, for the applicable qualification requirements for the specific high complexity subspecialties for the general supervisor.

493.1463 Standard: General Supervisor Responsibilities

The GS must be available to testing personnel at all times testing is performed (on-site, telephone, or electronic). The GS is responsible for providing day-to-day supervision of high complexity test performance by testing personnel, and monitoring test analyses and specimen examinations to ensure acceptable levels of analytic performance are maintained. If the director or TS chooses, the GS assures all remedial actions are taken, ensures results are not reported until the test system is properly functioning, provides orientation to testing personnel, and annually evaluates and documents personnel performance.

493.1487 Condition: Laboratories Performing Non-waived, (High Complexity Testing); Testing Personnel

The laboratory must have a sufficient number of individuals who meet the qualification requirements.

493.1489 Standard; Testing Personnel Qualifications

Each individual must possess a current license issued in the state where the laboratory is located, if required, be a doctor of medicine or osteopathy duly licensed, 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, have earned an associate degree in a chemical, physical, biological or medical laboratory technology from an accredited institution.

NOTE: Please refer to the CLIA regulation, for the applicable qualification requirements for the specific high complexity subspecialties for testing personnel.

493.1495 Standard; Testing Personnel Responsibilities

Testing personnel are responsible for specimen processing, test performance, and reporting test results. Each individual performs only those high complexity tests that are authorized by the director and require a degree of skill commensurate with the individual's education, training, and technical abilities. Testing personnel must follow laboratory procedures, maintain records for testing of PT samples, adhere to the laboratory's QC policies, be capable of identifying problems and either corrects them or notify the appropriate person, and document all corrective actions.

Subpart Q

Inspection

493.1775 Condition: Inspection of Laboratories Issued a Certificate of Waiver

An unannounced inspection of the laboratory by HHS or its designee can occur any time. The laboratory must allow HHS: to interview all laboratory employees to assess compliance, to inspect all areas of the facility, to observe employees, and to request data and information in order to determine that testing is performed without public health risk. In addition, the laboratory must provide all records and data that are requested. If the laboratory refuses to permit an inspection, a suspension or termination of Medicare/Medicaid payments, and suspension of or action to revoke the laboratory's CLIA certificate of waiver will ensue.

493.1777 Condition: Inspection of All Laboratories Not Issued a Certificate of Waiver or a Certificate of Accreditation

HHS or its designee will conduct unannounced inspections at least biennially of any laboratory. HHS will inspect a laboratory possessing a registration certificate before issuance of a certificate. The laboratory may be required to test samples, allow HHS to interview and/or observe employees, inspect the facility, and provide all records and data that are requested (records are retained for at least two years). HHS may re-inspect a laboratory at any time necessary. If the laboratory refuses to permit an inspection, a suspension or termination of Medicare/Medicaid payments, and suspension of or action to revoke the laboratory's CLIA certificate of waiver will ensue.

493.1780 Condition: Inspection of Accredited and State-Exempt Laboratories

HHS or its designee will conduct unannounced validation inspections and complaint inspections of such laboratories. The laboratory may be required to test samples, allow HHS to interview and/or observe employees, inspect the facility, and provide all records and data that are requested (records are retained for at least two years). HHS may re-inspect a laboratory at any time necessary. If the laboratory refuses to permit an inspection, a suspension or termination of Medicare/Medicaid payments, and suspension of or action to revoke the laboratory's CLIA certificate of accreditation will ensue.

Subpart T

Consultations

493.2001 Establishment and Function of the Clinical Laboratory Improvement Advisory Committee (CLIAC)

A CLIAC will be established by HHS to advise and make technical recommendations concerning criteria for categorizing non-waived, categorizing of waived tests, personnel standards, QA/QC standards, patient test management, PT standards, and applicability of new technology to the standards. This committee will include individuals involved in the provision of laboratory services, utilization of laboratory services, development of test systems or methodologies, or others. Specialized subcommittees may be formed. All committees must meet at least once a year. HHS will be responsible for providing information or data to the CLIAC.

Proficiency Testing Agencies

College of American Pathologists
325 Waukegan Road
Northfield, IL 60093-2750
FL Surveys
www.cap.org

UK NEQAS for Leucocyte Immunophenotyping
Rutledge Mews,
3 Southbourne Road, Sheffield,
S10 2QN

Tel: +44 (0)114 2673602
Fax: +44 (0)114 2673601

Flow Cytometry Quality Control

Flow cytometry covers a wide variety of applications ranging from the enumeration of Lymphocyte subsets and CD34 stem and progenitor cells, DNA cell cycle analysis, functional assays and the Leukemia/lymphoma immunophenotyping. The laboratory is responsible for designing a quality control parameters for each type of assay based on the quality requirements, whether it is qualitative or quantitative and the availability of control material. Quality control in flow cytometry includes the following:

- Instrument QC (Flow cytometer)
- Other equipment function checks
- Antibody QC
- Reagent QC
- Procedural/Method QC
- Internal/Patient QC
- Specimen integrity verifications

Instrument (Flow Cytometer) QC:

Instrument QC will depend on the flow cytometer manufacturer, make, model and whether the instrument is built for clinical or research use. Generally speaking the instrument manufacturer will set up and optimize the instrument for the lab needs with respect to optical alignment, photomultiplier standardization, sensitivity, linearity and compensation. It is then the laboratory's responsibility to monitor these parameters on a daily basis to ensure instrument stability. This is performed with stable microbeads with measurable fluorescence and light scatter signals in addition to preserved or fresh cells.

The optical alignment QC optimizes the sample stream with the path of the laser beam and collection bins. Commercially available microbeads are available for this process. Target values are the "brightest and tightest" peak for each channel. In other words, the target is the highest fluorescent channel with the lowest %CV (<2%).

The standardization QC verifies that flow cytometer has the same fluorescent and light scatter for each protocol each day of use. Commercially available microbeads are available for this process. This can be performed one of two ways; by monitoring the bead mean fluorescent intensity and light scatter channel each day of use and plotting overtime, or instrument software adjusts the PMT voltages to place each fluorescent and light scatter channel in the same position each day, monitoring the changes in voltages and plotting these over time. Monitoring trends or shifts can identify instrument problems.

Compensation QC corrects for spectral overlap of one fluorochrome into the fluorescent spectrum of another. Commercially available microbeads are available for this process for some systems. Many applications require further optimization with preserved or fresh cells.

Linearity/sensitivity QC verifies that each detector has a linear response. It also verifies the ability to distinguish dim positive signal from negative signal. Commercially available microbeads are available for this process. Acceptability criteria will depend on the application.

Other equipment function checks

All other equipment used in the flow cytometry laboratory must have manufacturers recommended function checks performed and documented. This includes temperature verification of temperature dependent equipment, centrifuge RPM verification, certification, of biohazard containment hoods, pipette calibration, etc. All function checks must be recorded and if out of an acceptable range, corrective action taken and documented prior to using the equipment.

Antibody QC

The purpose of this QC is to verify the antibody reactivity from lot to lot is consistent and also to verify the antibodies are labeling the target population as expected. (see procedural QC). Each new antibody lot must be tested for equivalency prior to use. One can use previously tested patient samples, cultured cells or commercial controls. Defined acceptability criteria must be attained and documented.

Reagent QC

Other critical reagents used in flow cytometry should be verified for equivalency prior to putting a new lot in use. Phasing in selected reagents will depend on the application and is determined by the laboratory director. Defined acceptability criteria must be attained and documented.

Procedural/Method QC

A procedural/method control is used to verify the entire analytical testing process is controlled each day of use. This control can also assess compensation and serve as an antibody QC. For quantitative assays such as CD34 and lymphocyte subsets, commercial controls are recommended with two levels; one normal and one at a clinical decision point. Monitoring these controls against established ranges and tracking values over time identifies assay problems. For simple qualitative assays, a positive and negative control should be run with each testing batch. This can be a commercial control or previously tested patient samples. Defined acceptability criteria must be attained and documented. For more complex qualitative assays such as leukemia and lymphoma immunophenotyping, a separate normal process control is not required. Most samples contain a component of normal cells providing data on the assay and reagent performance. Panels must be configured such that normal cells have distinct negative and positive controls. These internal controls can serve as positive and negative controls for each antibody. If internal controls are used, acceptability criteria must be established, results documented as well as corrective action documented if problems occur.

Internal/Patient QC

Many flow cytometry contain internal checks and balances that can be used as additional QC checks. For lymphocyte subset enumeration, the lympho-sum (CD3+NK+CD19) should account for all the gated lymphocytes in the sample and approach 100%. In addition, the T sum (CD4+ T

cells + CD8+ T cells) should approach the total CD3. In addition, duplicate markers run on the same patient should be equivalent (example replicate CD3). If using single platform technology (SPT) time should be constant when acquiring multiple tubes on the same patient. Using these internal/patient QC parameters can identify potential assay problems.

The important aspects to note are that the laboratory is responsible for the design and effectiveness of the quality control program. All parameters being checked must have stated tolerance limits and all work must be reviewed periodically by the laboratory director.

Flow Cytometry Quality Assessment (QA)

Quality assessment in flow cytometry ensures that the immediate and ultimate customers of the laboratory service (clinicians and patients), that the results are precise and clinically accurate. QA includes assay validation, document and change control of procedures, pre and post analytical sample handling such as specimen labeling and inadequate samples, and reporting turn around time. Laboratories should perform a detailed review of all these processes with the goals of incremental improvement and elimination of waste. Some examples of major components of quality assessment in clinical flow cytometry are as follows:

- Specimen collection/rejection criteria:
- Clinical information
- Sample preparation
- Specimen integrity verifications
- Data acquisition
- Data analysis
- Interpretation/reporting
- Training and ongoing competency
- Quality improvement

Specimen collection/rejection criteria:

Good laboratory practice states that the specimen containers be labeled at the point of collection. Samples must be submitted to the testing laboratory with a formal test request/order. In flow cytometry the date and time of collection is critical. The sample must be drawn in the appropriate anticoagulant with appropriate volume. Sample storage and shipping temperatures are also critical and can adversely affect results. The laboratory must document sample rejection criteria and act upon suboptimal sample receipt. Specimen collection errors can be tracked and monitored as a quality improvement.

Clinical information

Depending on the flow cytometry assay, clinical information is critical to accurate results. For enumeration of lymphocyte subsets and CD34 cells, this information may not be as critical as leukemia/lymphoma immunophenotyping. For the latter, clinical indication will provide the laboratory information on how to proceed with the procedure.
Sample preparation

Specimen integrity verifications

Flow cytometry testing measures the presence of antigens on the surface of the viable cells. Accuracy depends on the viability of the sample received. In some applications, an assessment of the percent of viable cells will identify situations where the results are not accurate. In flow cytometry assays the ratio of cells of interest (antigen) and amount of antibody must be

optimized for best results and consistent for reproducibility. In many tests, the cell count of the patient sample is reviewed and adjusted (if needed) to optimize this ratio.

Data acquisition

In many flow cytometric assays, the number of acquired events must be robust enough for clinically relevant precision. This is generally defined by the assay quality requirements. For example, CD34 stem cell assays require a minimum of 100 cells of interest to assure an appropriate CV. For leukemia/lymphoma analysis, depending on the cell lineage of interest and required sensitivity the amount of acquired events may vary.

Data analysis

During the flow cytometric analysis step the gating technique is critical to identify the population of interest. Gating techniques are application specific and may require gating on light scatter or a combination of light scatter and fluorescence. Appropriate gating techniques can optimize the sensitivity of the assay. Data analysis in flow cytometry may require a qualitative assessment of the antigen expression (positive or negative) or a semi quantitative approach where the fluorescent intensity is assessed as compared to normal cell counterparts (dim or bright).

Interpretation/reporting

In quantitative flow cytometry assays clinicians are the ones that interpret the numerical value reported. This is the case for CD4 and CD34 measurements. In other applications such as leukemia/lymphoma immunophenotyping, a pathologist will interpret the case based on the qualitative pattern recognition of abnormal cells. This in conjunction with clinical indication and other laboratory results will ensure appropriate results.

Training and ongoing competency

All technical laboratory staff require adequate training on all job assignments. This training must be performed by a qualified trainer, with specific criteria for acceptability and sign off. Training verification is documented and approved by the supervisor and trainee. Any modifications or remedial problems require additional documented training. Ongoing competency assessment is verifying that the once trained, staff continue to perform the job assignment appropriately and meet objective minimum standards. Competency assessment must be performed and documented within the first six months and annually thereafter. Multiple modalities of assessment must be used ; direct observation, records review, blind testing and problem solving. Competency assessments must have objective criteria and be reviewed by the technical supervisor.

Quality improvement

Quality improvement is a process in a clinical laboratory that measures the nonconformance's to procedures and identifies areas that need improvement. Example quality improvement metrics in flow cytometry may be turnaround time, sample handling errors, client complaints, delayed shipping, corrected or amended reports. Root cause analysis can identify potential causes and solutions. These must be documented and communicated to laboratory staff.

PROFICIENCY TESTING (PT) SURVEY LISTING

& PARTICIIPATION SUMMARY FORM

Institution:	Department:
Survey Year:	PT Supplier:
Suppliers Phone #:	Instrument #:

SURVEY NAME	ANALYTE	SHIPMENT DATES

Prepared by:	Date:
Reviewed by:	Date:

Condition: 493.801

FORM FC-2

PROFICIENCY TESTING (PT) PROCESSING FORM ENROLLMENT AND TESTING OF SAMPLES: FLOW CYTOMETERY			
Institution:		**Department:**	
PT Supplier	**Survey Year:**	**Survey Name:**	
Supplier Phone #:		**Results Due Date:**	
Received at Testing Site by:			
Date:		**Time:**	
Received in Acceptable Condition:		**Y:**	**N:**
If Not, Action Taken:			
Signature		**Date:**	**Time:**
Results Acceptable:		**Yes:**	**No:** **Score:**
Action Required (Form FC-3):		**Y:**	**N:**

PT Sample	Analyte(s)	Result(s) Reported	Correct Result(s)

Prepared by:	**Date:**
Reviewed by:	**Date:**

Conditions: 493.801/493.821/493.833/493.839

FORM FC-3

REMEDIAL ACTION FORM
UNACCEPTABLE PROFICIENCY TESTING RESULTS
FLOW CYTOMETRY

Institution:	**Department:**
Survey Year:	**Shipment Date:**
PT Supplier:	**Results Due Date:**

Reasons for Unacceptable Results:

Explanation of Incident:

Prepared by:	**Date:**

Remedial Action Taken:

Prepared by:	**Date:**

Results of Remedial Action Taken:

Prepared by:	**Date:**
Reviewed by:	**Date:**

Conditions: 493.821/493.833/493.839

FORM FC-4

QUALITY ASSURANCE REVIEW FORM
EVALUATION OF CORRECTIVE ACTIONS ON
UNSATISFACTORY PROFICIENCY TESTING RESULTS

Institution:		**Department:**			
PT Supplier		**Survey Year:**		**Survey Name:**	
DATE OF PT	**SAMPLE**	**REPORTED RESULT**	**ACCEPTABLE RESULT**	**ACTION TAKEN (Y/N)**	**ACTION DOCUMENTED (Y/N)**
Prepared by:				**Date:**	
Reviewed by:				**Date:**	

Standard: 493.1707

FORM FC-5A

CYTOMETRY EQUIPMENT AND FUNCTION CHECKS FORM

INSTRUMENT #:	MONTH:	YEAR:

Beads Lot #_____ Expiration_____

Day of the Month		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Parameter	Range																															

Reviewed by: ***Date:***

Standard: 493.1215

FORM FC-5B

LABORATORY EQUIPMENT AND FUNCTION CHECKS FORM

MONTH:	YEAR:

Day of the Month		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Parameter	Range																															

Reviewed by: ***Date:***

Standard: 493.1215

FORM FC-5C

CORRECTIVE ACTION FORM
PREVENTIVE MAINTENANCE AND FUNCTION CHECKS

Institution:	**Department:**
Equipment:	
Procedure:	

Description of Problem: _____

Prepared by:	**Date:**

Corrective Action Taken: _____

Prepared by:	**Date:**

Comments: _____

Reviewed by:	**Date:**

Standard: 493.1215

FORM FC-5D

EQUIPMENT SERVICE LOG

DATE	PROBLEM	TECH	DATE	ACTION TAKEN	TECH

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1219

FORM FC-6

PIPETTE CALIBRATION FORM

Institution:	**Department:**
Pipette #:	**Acceptable Range:**
Calibration Method: Gravimetric	
Balance Used:	
Evaporation Factor:	**Acceptable Results?: Y N**
Placed in Service?: Y Date:	**Discarded Date:**

CALIBRATION RESULTS

#	Replicates		Calculations
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
	Mean=		**Mean – Evap Factor =**
			Accuracy = Mean Volume – Ideal Volume x 100 = % Ideal Volume

USE ADDITIONAL PAGES AS NEEDED

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standards: 493.121

_____

ADEQUACY OF METHODS/EQUIPMENT/INSTRUMENTS FOR TESTING

Institution:	**Date:**
Department:	**Test:**
Method:	

Cleared by FDA; Meets CLIA '88 Requirements for General QC: Y / N

CHART OF PARAMETERS

	Manufacturer's Technical Information	Laboratory Data
Reportable Range		
Reference Range		
Specimen of Choice		
Precision		
Accuracy		
Analytical Sensitivity		
Analytical Specificity		
Interfering Substances		
Special Considerations		
Other		
Therapeutic Range		

Summary of Adequacy:

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1213

FORM FC-8

QUALITY CONTROL FORM

INSTRUMENT:	MONTH:	YEAR:

Date Tested	QC Material Used	Lot/ Exp.	CD Control Value	CD Control Expected Range	CD Control Value	CD Control Expected Range	CD Control Value	CD Control Expected Range	Technician

.

Standard: 493.1218

FORM FC-9

REMEDIAL ACTION FORM TEST RESULTS REPORTED IN ERROR		
Institition:	**Department:**	
Patient Name:		
Patient ID:	**Accession #:**	
Date Specimen Collected:	**Time Specimen Collected:**	
Test:		
Incorrect Result:		
Corrected Result:		
Description of Incident:		
Person Notified of Incident:		
Notification Date:	**Notification Time:**	**By:**
Corrective Action Taken:		
Prepared by:		**Date:**
Corrected Result Reported to:		
Date:	**Time:**	
Method:		
Prepared by:		**Date:**
Reviewed by:		**Date:**

Standard: 493.1219

FORM FC-10

QUALITY ASSURANCE REVIEW CRITERIA FOR SPECIMEN COLLECTION AND HANDLING	
Institution:	**Department:**
QA Review Month:	**QA Review Year:**

✓	TYPE OF REVIEW (CRITERIA FOR):	ACTION TAKEN ✓
	Patient Preparation	
	Specimen Collection	
	Labeling	
	Preservation	
	Transportation	

Dates for Data Collection:				
Shifts:	**1**	**2**	**3**	**All**
Number of Specimens Received:		**=**	**100 %**	
Number of Specific Problems:		**=**	**%**	
Evaluation of Criteria: _____				

Problem Target % = < _____%

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1703

FORM FC-11

QUALITY ASSURANCE REVIEW FORM
EVALUATION OF CRITERIA FOR SPECIMEN REJECTION

Institution:	**Department:**
QA Review Month:	**QA Review Year:**
Total # of Reviewed Specimens:	**Total # Unacceptable Specimens:**
% Unacceptable Specimens:	**Unacceptable Specimen Target: _____ %**

DATE	PATIENT ID	REASON FOR UNACCEPTABILITY	SAMPLE TESTED (Y/N)	USER NOTIFIED (Y/N)

Evaluation of Effectiveness: _____

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1703

FORM FC-12

QUALITY ASSURANCE REVIEW FORM
COMPLETENESS OF INFORMATION ON REQUISITIONS AND REPORTS

Institution:	**Department:**
QA Review Month:	**QA Review Year:**

REQUISITION			REPORT FORM		
✓	TYPE OF REVIEW	ACTION TAKEN ✓	✓	TYPE OF REVIEW	ACTION TAKEN ✓
	Patient Name			Patient Name	
	Location			Location	
	I.D. #			I.D. #	
	Ordering Physician			Ordering Physician	
	Test Ordered			Test Ordered	
				Normal Range	
				Interpretation	
				Lab Med. Director	

Dates for Data Collection:

Shifts: 1 2 3 All

Number of Requisitions or Reports Reviewed: _____ **= 100%**

Number of Missing Items under Review: _____ **=** _____**% Incompleteness**

Evaluation of Completeness: _____

Incompleteness Target % = < _____**%**

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1703

FORM FC-13

QUALITY ASSURANCE REVIEW FORM
QUALITY ASSURANCE FOR QUALITY CONTROL CORRECTIVE ACTIONS

Institution:	**Department:**
QA Review Month:	**QA Review Year:**

✓	TYPE OF REVIEW	ACTION TAKEN ✓
	Problems identified during the evaluation of calibration and control data for each test method	
	Problems identified during the evaluation of patient test values for the purpose of verifying the reference range of a test method	
	Errors detected in reported results	
	Other: _____	

Problem/Error Target % = < _____%

Total # Reviewed:

# of Problems/Errors:_____	**% of Problems/Errors: _____ %**

Evaluation of Effectiveness: _____

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1705

FORM FC-14

QUALITY ASSURANCE REVIEW FORM
RELATIONSHIP BETWEEN TEST RESULTS USING DIFFERENT METHODS, INSTRUMENTS OR TESTING SITES

Institution:	**Department:**
Test System #1:	**Test System #2:**
Test Site:	**Test Site:**
Methodology:	**Methodology:**
Instrument:	**Instrument:**
Identification Number:	**Identification number:**
Normal Range:	**Normal Range:**

For Quantitative Assays:

Obtained Correlation Coefficient = _____

Acceptable Correlation Coefficient = > _____

Acceptable Delta = _____

Date	Sample #	Test System # 1	Test System # 2	Delta	Acceptable Y/N	Tester

USE ADDITIONAL PAGES AS NEEDED

Evaluation of Relationship:

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1709

FORM FC-15

QUALITY ASSESSMENT REVIEW FORM
EVALUATION OF PATIENT TEST RESULTS
INCONSISTENT WITH PATIENT CRITERIA

Institution:	**Department:**
Total # of Results Reviewed:	**# of Inconsistent Results Evaluated:**
% Inconsistent Results Evaluated:	**Target % Evaluation:**

			RESULTS INCONSISTENT WITH:				
DATE	# OF RESULTS	SHIFT	OTHER TESTS	RESULT DISTRIBUTION	DIAGNOSIS	AGE	SEX

Evaluation of Inconsistencies: _____

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1711

FORM FC-16 ☐ **SEE ATTACHED SHEET(S)**

QUALITY ASSESSMENT REVIEW FORM
EMPLOYEE QUALIFICATION DOCUMENTATION

Institution:	**Department:**

EMPLOYEE NAME	POSITION	DATE HIRED	QUALIFICATION ROUTE AS DESCRIBED IN 493.1443-1489
	Director		
	Technical Supervisor		
	Clinical Consultant		
	General Supervisor		
	Testing Personnel		

Note: The same individual may serve several roles in the laboratory, if qualified.

Copies of all degrees and certification, if applicable, are attached to this form.

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1443-1489

QUALITY ASSESSMENT REVIEW FORM
EMPLOYEE COMPETENCE REVIEW-FLOW CYTOMETRY

Institution:	**Department:**

EMPLOYEE NAME	TECHNICAL SUPERVISOR	COMPETENCY VALIDATION METHOD **A. Direct Observation of Routine Testing** B. MONITORING TEST RESULTS C. REVIEW OF WORKSHEETS, QC, ETC. D. DIRECT OBSERVATION OF INSTRUMENT MAINTENANCE E. TESTING OF BLIND SAMPLES OR PROFICIENCY TESTS F. ASSESSMENT OF PROBLEM SOLVING ABILITY

Prepared by:	**Date:**
Reviewed by:	**Date:**

Condition: 493.1451

FORM FC-18 **FORM _____ OF ___**

☐ **SEE DOCUMENTATION ATTACHED**

QUALITY ASSESSMENT REVIEW FORM
DOCUMENTATION OF COMPLAINTS AND PROBLEMS REPORTED TO LABORATORY

Institution:	**Department:**
Review Month:	**Review Year:**

REASON FOR COMPLAINT/INCIDENT REPORT

Explanation of Incident: **(Date: _____ Time: _____)**

Prepared by:	**Date:**

Corrective Action Taken: _____

Prepared by:	**Date:**

Results of Corrective Action Taken: _____

Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1717

FORM FC-19

QUALITY ASSESSMENT REVIEW FORM
QUALITY ASSESSMENT REVIEW WITH STAFF

Institution:	**Department:**
Staff Members Present/Contacted:	
Problems Identified in QA Reports:	
Prepared by:	**Date:**
Corrective Action Taken:	
Prepared by:	**Date:**
Results of Corrective Action Taken:	
Prepared by:	**Date:**
Reviewed by:	**Date:**

Standard: 493.1719