

| Examinee's response:       | A  | B  | C  | D  |
|----------------------------|----|----|----|----|
| Correct response category: |    |    |    |    |
| A .....                    | 10 | 0  | 5  | 5  |
| B .....                    | 5  | 10 | 5  | 5  |
| C .....                    | 5  | 0  | 10 | 10 |
| D .....                    | 0  | -5 | 10 | 10 |

(E) In accordance with the criteria for the scoring system, the charts in paragraphs (b)(3)(ii)(F) and (G) of this section, for technical supervisors and cytotechnologists, respectively, provide maximums of 5 points for a correct response and minus ten (-10) points for an incorrect response on a 20-slide test set.

(F) Criteria for scoring system for a 20-slide test set. (See table at paragraph (b)(3)(ii)(A) of this section for a description of the response categories.) For technical supervisors qualified under § 493.1449(b) or (k):

| Examinee's response:       | A   | B   | C   | D   |
|----------------------------|-----|-----|-----|-----|
| Correct response category: |     |     |     |     |
| A .....                    | 5   | 0   | 0   | 0   |
| B .....                    | 2.5 | 5   | 0   | 0   |
| C .....                    | 2.5 | 0   | 5   | 2.5 |
| D .....                    | 0   | -10 | 2.5 | 5   |

(G) Criteria for scoring system for a 20-slide test set. (See table at (b)(3)(ii)(A) of this section for a description of the response categories.) For cytotechnologists qualified under §§ 493.1469 or 493.1483:

| Examinee's response:       | A   | B   | C   | D   |
|----------------------------|-----|-----|-----|-----|
| Correct response category: |     |     |     |     |
| A .....                    | 5   | 0   | 2.5 | 2.5 |
| B .....                    | 2.5 | 5   | 2.5 | 2.5 |
| C .....                    | 2.5 | 0   | 5   | 5   |
| D .....                    | 0   | -10 | 5   | 5   |

[57 FR 7151, Feb. 28, 1992, as amended at 58 FR 5229, Jan. 19, 1993; 68 FR 3702, Jan. 24, 2003]

**§ 493.959 Immunohematology.**

(a) *Types of services offered by laboratories.* In immunohematology, there are four types of laboratories for proficiency testing purposes—

- (1) Those that perform ABO group and/or D (Rho) typing;
- (2) Those that perform ABO group and/or D (Rho) typing, and unexpected antibody detection;
- (3) Those that in addition to paragraph (a)(2) of this section perform compatibility testing; and

(4) Those that perform in addition to paragraph (a)(3) of this section anti-body identification.

(b) *Program content and frequency of challenge.* To be approved for proficiency testing for immunohematology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the full range of interpretation that would be expected in patient specimens. The samples may be provided through mailed shipments or, at HHS' option, may be provided to HHS or its designee for on-site testing.

(c) *Challenges per testing event.* The minimum number of challenges per testing event a program must provide for each analyte or test procedure is five.

*Analyte or Test Procedure*

- ABO group (excluding subgroups)
- D (Rho) typing
- Unexpected antibody detection
- Compatibility testing
- Antibody identification

(d) *Evaluation of a laboratory's analyte or test performance.* HHS approves only those programs that assess the accuracy of a laboratory's response in accordance with paragraphs (d)(1) through (5) of this section.

(1) To determine the accuracy of a laboratory's response, a program must compare the laboratory's response for each analyte with the response that reflects agreement of either 100 percent of ten or more referee laboratories or 95 percent or more of all participating laboratories except for unexpected antibody detection and antibody identification. To determine the accuracy of a laboratory's response for unexpected antibody detection and antibody identification, a program must compare the laboratory's response for each analyte with the response that reflects agreement of either 95 percent of ten or more referee laboratories or 95 percent or more of all participating laboratories. The score for a sample in immunohematology is either the score determined under paragraph (d)(2) or (3) of this section.

(2) *Criteria for acceptable performance.* The criteria for acceptable performance are—

| Analyte or test                     | Criteria for acceptable performance |
|-------------------------------------|-------------------------------------|
| ABO group .....                     | 100% accuracy.                      |
| D (Rho) typing .....                | 100% accuracy.                      |
| Unexpected antibody detection ..... | 80% accuracy.                       |
| Compatibility testing .....         | 100% accuracy.                      |
| Antibody identification .....       | 80% accuracy.                       |

(3) The criterion for acceptable performance for qualitative immunohematology tests is positive or negative.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

$$\frac{\text{Number of acceptable responses for the analyte} \times 100}{\text{Analyte score for the testing event}}$$

-----  
 Total number of challenges for the analyte

(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

$$\frac{\text{Number of acceptable responses for all challenges} \times 100}{\text{Testing event score}}$$

-----  
 Total number of all challenges

**Subpart J—Facility Administration for Nonwaived Testing**

SOURCE: 68 FR 3703, Jan. 24, 2003, unless otherwise noted.

**§ 493.1100 Condition: Facility administration.**

Each laboratory that performs non-waived 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 (CMS Pub. 7).

**§ 493.1101 Standard: Facilities.**

(a) The laboratory must be constructed, arranged, and maintained to ensure the following:

(1) The space, ventilation, and utilities necessary for conducting all phases of the testing process.

(2) Contamination of patient specimens, equipment, instruments, reagents, materials, and supplies is minimized.

(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.

(b) The laboratory must have appropriate and sufficient equipment, instruments, reagents, materials, and supplies for the type and volume of testing it performs.

(c) The laboratory must be in compliance with applicable Federal, State, and local laboratory requirements.

(d) Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials.

(e) Records and, as applicable, slides, blocks, and tissues must be maintained and stored under conditions that ensure proper preservation.

**§ 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.

(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.

(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.

(c) *Blood and blood products storage and distribution.* (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.

(2) The facility must establish and follow policies to ensure positive identification of a blood or blood product recipient.

(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.

**§ 493.1105 Standard: Retention requirements.**

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

(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.

(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.

(3) *Analytic systems records.* Retain quality control and patient test records (including instrument printouts, if applicable) and records documenting all analytic systems activities specified in §§ 493.1252 through 493.1289 for at least 2 years. In addition, retain the following:

(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.

(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).

(4) *Proficiency testing records.* Retain all proficiency testing records for at least 2 years.

(5) *Quality system assessment records.* Retain all laboratory quality systems assessment records for at least 2 years.

(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:

(i) Immunohematology reports as specified in 21 CFR 606.160(d).

(ii) Pathology test reports for at least 10 years after the date of reporting.

(7) *Slide, block, and tissue retention—(i) Slides.* (A) Retain cytology slide preparations for at least 5 years from the date of examination (see § 493.1274(f) for proficiency testing exception).

(B) Retain histopathology slides for at least 10 years from the date of examination.

(ii) *Blocks.* Retain pathology specimen blocks for at least 2 years from the date of examination.

(iii) *Tissue.* Preserve remnants of tissue for pathology examination until a diagnosis is made on the specimen.

(b) If the laboratory ceases operation, the laboratory must make provisions to ensure that all records and, as applicable, slides, blocks, and tissue are retained and available for the time frames specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50723, Aug. 22, 2003]

### Subpart K—Quality System for Nonwaived Testing

SOURCE: 68 FR 3703, Jan. 24, 2003, unless otherwise noted.

**§ 493.1200 Introduction.**

(a) Each laboratory that performs nonwaived testing must establish and maintain written policies and procedures that implement and monitor a quality system 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 components 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.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 493.1207 Condition: Syphilis serology.**

If the laboratory provides services in the subspecialty of Syphilis serology, the laboratory must meet the require-

ments specified in §§ 493.1230 through 493.1256, and §§ 493.1281 through 493.1299.

**§ 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.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

**§ 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.

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 §§ 493.1231 through 493.1236, un-

less 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 § 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 person who orders or receives test results.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.**

(a) The laboratory must review and evaluate the results obtained on proficiency testing performed as specified in subpart H of this part.

(b) The laboratory must verify the accuracy of the following:

(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.

(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 of results).

(c) At least twice annually, the laboratory must verify the accuracy of the following:

(1) Any test or procedure it performs that is not included in subpart I of this part.

(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.

(d) All proficiency testing evaluation and verification activities must be documented.

**§ 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.

(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.

(c) The laboratory must document all general laboratory systems quality assessment activities.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

## PREANALYTIC SYSTEMS

**§ 493.1240 Condition: Preanalytic systems.**

Each laboratory that performs non-waived 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 (CMS Pub. 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.

**§ 493.1241 Standard: Test request.**

(a) The laboratory must have a written or electronic request for patient testing from an authorized person.

(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.

(c) The laboratory must ensure the test requisition solicits the following information:

(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.

(2) The patient's name or unique patient identifier.

(3) The sex and age or date of birth of the patient.

(4) The test(s) to be performed.

(5) The source of the specimen, when appropriate.

(6) The date and, if appropriate, time of specimen collection.

(7) For Pap smears, the patient's last menstrual period, and indication of whether the patient had a previous abnormal report, treatment, or biopsy.

(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.

(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.

(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.

**§ 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:

- (1) Patient preparation.
- (2) Specimen collection.
- (3) Specimen labeling, including patient name or unique patient identifier and, when appropriate, specimen source.
- (4) Specimen storage and preservation.
- (5) Conditions for specimen transportation.
- (6) Specimen processing.
- (7) Specimen acceptability and rejection.
- (8) Specimen referral.

(b) The laboratory must document the date and time it receives a specimen.

(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.

(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.

**§ 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.

(b) The preanalytic 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 preanalytic systems quality assessment reviews with appropriate staff.

(c) The laboratory must document all preanalytic systems quality assessment activities.

[68 FR 3703, Jan. 24, 2003; 68 FR 3703, Aug. 22, 2003]

ANALYTIC SYSTEMS

**§ 493.1250 Condition: Analytic systems.**

Each laboratory that performs non-waived 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 (CMS Pub. 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.

**§ 493.1251 Standard: Procedure manual.**

(a) A written procedure 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.

(b) The procedure manual must include the following when applicable to the test procedure:

- (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.

(2) Microscopic examination, including the detection of inadequately prepared slides.

(3) Step-by-step performance of the procedure, including test calculations and interpretation of results.

(4) Preparation of slides, solutions, calibrators, controls, reagents, stains, and other materials used in testing.

(5) Calibration and calibration verification procedures.

(6) The reportable range for test results for the test system as established or verified in § 493.1253.

(7) Control procedures.

(8) Corrective action to take when calibration or control results fail to meet the laboratory's criteria for acceptability.

(9) Limitations in the test methodology, including interfering substances.

(10) Reference intervals (normal values).

(11) Imminently life-threatening test results, or panic or alert values.

(12) Pertinent literature references.

(13) The laboratory's system for entering results in the patient record and reporting patient results including, when appropriate, the protocol for reporting imminently life-threatening results, or panic, or alert values.

(14) Description of the course of action to take if a test system becomes inoperable.

(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.

(d) Procedures and changes in procedures must be approved, signed, and dated by the current laboratory director before use.

(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).

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.

(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:

(1) Water quality.

(2) Temperature.

(3) Humidity.

(4) Protection of equipment and instruments from fluctuations and interruptions in electrical current that adversely affect patient test results and test reports.

(c) Reagents, solutions, culture media, control materials, calibration materials, and other supplies, as appropriate, must be labeled to indicate the following:

(1) Identity and when significant, titer, strength or concentration.

(2) Storage requirements.

(3) Preparation and expiration dates.

(4) Other pertinent information required for proper use.

(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.

(e) Components of reagent kits of different lot numbers must not be interchanged unless otherwise specified by the manufacturer.

**§ 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.

(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:

(i) Demonstrate that it can obtain performance specifications comparable to those established by the manufacturer for the following performance characteristics:

(A) Accuracy.

(B) Precision.

(C) Reportable range of test results for the test system.

(ii) Verify that the manufacturer's reference intervals (normal values) are appropriate for the laboratory's patient population.

(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:

(i) Accuracy.

(ii) Precision.

(iii) Analytical sensitivity.

(iv) Analytical specificity to include interfering substances.

(v) Reportable range of test results for the test system.

(vi) Reference intervals (normal values).

(vii) Any other performance characteristic required for test performance.

(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.

(c) *Documentation.* The laboratory must document all activities specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 493.1254 Standard: Maintenance and function checks.**

(a) *Unmodified manufacturer's equipment, instruments, or test systems.* The laboratory must perform and document the following:

(1) Maintenance as defined by the manufacturer and with at least the frequency specified by the manufacturer.

(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.

(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:

(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.

(ii) Perform and document the maintenance activities specified in paragraph (b)(1)(i) of this section.

(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.

(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.

**§ 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:

(a) Perform and document calibration procedures—

(1) Following the manufacturer's test system instructions, using calibration materials provided or specified, and with at least the frequency recommended by the manufacturer;

(2) Using the criteria verified or established by the laboratory as specified in § 493.1253(b)(3)—

(i) Using calibration materials appropriate for the test system and, if possible, traceable to a reference method or reference material of known value; and

(ii) Including the number, type, and concentration of calibration materials, as well as acceptable limits for and the frequency of calibration; and

(3) Whenever calibration verification fails to meet the laboratory's acceptable limits for calibration verification.

(b) Perform and document calibration verification procedures—

(1) Following the manufacturer's calibration verification instructions;

(2) Using the criteria verified or established by the laboratory under § 493.1253(b)(3)—

(i) Including the number, type, and concentration of the materials, as well as acceptable limits for calibration verification; and

(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

(3) At least once every 6 months and whenever any of the following occur:

(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.

(ii) There is major preventive maintenance or replacement of critical parts that may influence test performance.

(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.

(iv) The laboratory's established schedule for verifying the reportable range for patient test results requires more frequent calibration verification.

**§ 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—

(1) Detect immediate errors that occur due to test system failure, adverse environmental conditions, and operator performance.

(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.

(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—

(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.

(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.

(3) At least once each day patient specimens are assayed or examined perform the following for—

(i) Each quantitative procedure; include two control materials of different concentrations;

(ii) Each qualitative procedure, include a negative and positive control material;

(iii) Test procedures producing graded or titered results, include a negative control material and a control material with graded or titered reactivity, respectively;

(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

(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.

(4) For thin layer chromatography—

(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

(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.

(5) For each electrophoretic procedure include, concurrent with patient specimens, at least one control material containing the substances being identified or measured.

(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.

(7) Over time, rotate control material testing among all operators who perform the test.

(8) Test control materials in the same manner as patient specimens.

(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.

(10) Establish or verify the criteria for acceptability of all control materials.

(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.

(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.

(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.

(e) For reagent, media, and supply checks, the laboratory must do the following:

(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.

(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.

(3) Check fluorescent and immunohistochemical stains for positive and negative reactivity each time of use.

(4) Before, or concurrent with the initial use—

(i) Check each batch of media for sterility if sterility is required for testing;

(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

(iii) Document the physical characteristics of the media when compromised and report any deterioration in the media to the manufacturer.

(5) Follow the manufacturer's specifications for using reagents, media, and supplies and be responsible for results.

(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.

(g) The laboratory must document all control procedures performed.

(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.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 493.1261 Standard: Bacteriology.**

(a) The laboratory must check the following for positive and negative reactivity using control organisms:

(1) Each day of use for beta-lactamase methods other than Cefinase™.

(2) Each week of use for Gram stains.

(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.

(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.

(1) Each day tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

(2) The laboratory's zone sizes or minimum inhibitory concentration for control organisms must be within established limits before reporting patient results.

(c) The laboratory must document all control procedures performed, as specified in this section.

**§ 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.

(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).

(1) The laboratory must establish limits for acceptable control results.

(2) Each week tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

(3) The results for the control organism(s) must be within established limits before reporting patient results.

(c) The laboratory must document all control procedures performed, as specified in this section.

**§ 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).

(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).

(1) The laboratory must establish limits for acceptable control results.

(2) Each day tests are performed, the laboratory must use the appropriate control organism(s) to check the procedure.

(3) The results for the control organism(s) must be within established limits before reporting patient results.

(c) The laboratory must document all control procedures performed, as specified in this section.

**§ 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.

(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.

(c) Each month of use, the laboratory must check permanent stains using a fecal sample control material that will demonstrate staining characteristics.

(d) The laboratory must document all control procedures performed, as specified in this section.

**§ 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.

(b) The laboratory must document all control procedures performed, as specified in this section.

**§ 493.1267 Standard: Routine chemistry.**

For blood gas analyses, the laboratory must perform the following:

(a) Calibrate or verify calibration according to the manufacturer's specifications and with at least the frequency recommended by the manufacturer.

(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.

(c) Test one sample of control material each time specimens are tested unless automated instrumentation internally verifies calibration at least every 30 minutes.

(d) Document all control procedures performed, as specified in this section.

**§ 493.1269 Standard: Hematology.**

(a) For manual cell counts performed using a hemocytometer—

(1) One control material must be tested each 8 hours of operation; and

(2) Patient specimens and control materials must be tested in duplicate.

(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.

(c) For manual coagulation tests—

(1) Each individual performing tests must test two levels of control materials before testing patient samples and each time a reagent is changed; and

(2) Patient specimens and control materials must be tested in duplicate.

(d) The laboratory must document all control procedures performed, as specified in this section.

**§ 493.1271 Standard: Immunohematology.**

(a) *Patient testing.* (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).

(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.

(3) The laboratory must determine the D(Rho) type by testing unknown red cells with anti-D (anti-Rho) blood typing reagent.

(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), (b), (c), and (e); and 640.11(b).

(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.

(1) An audible alarm system must monitor proper blood and blood product storage temperature over a 24-hour period.

(2) Inspections of the alarm system must be documented.

(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.

(e) *Investigation of transfusion reactions.* (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.

(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.

(f) *Documentation.* The laboratory must document all control procedures performed, as specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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. Reaction(s) of the control slide with each special stain must be documented.

(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).

(c) An individual who has successfully completed a training program in neuromuscular pathology approved by HHS may examine and provide reports for neuromuscular pathology.

(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.

(e) The laboratory must use acceptable terminology of a recognized system of disease nomenclature in reporting results.

(f) The laboratory must document all control procedures performed, as specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.

(b) *Staining.* The laboratory must have available and follow written policies and procedures for each of the following, if applicable:

(1) All gynecologic slide preparations must be stained using a Papanicolaou or modified Papanicolaou staining method.

(2) Effective measures to prevent cross-contamination between gynecologic and nongynecologic specimens during the staining process must be used.

(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.

(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:

(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).

(i) The review must be performed by an individual who meets one of the following qualifications:

(A) A technical supervisor qualified under §§ 493.1449(b) or (k).

(B) A cytology general supervisor qualified under § 493.1469.

(C) A cytotechnologist qualified under § 493.1483 who has the experience specified in § 493.1469(b)(2).

(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.

(iii) The review of those cases selected must be completed before reporting patient results.

(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.

(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.

(4) Records of initial examinations and all rescreening results must be documented.

(5) An annual statistical laboratory evaluation of the number of—

- (i) Cytology cases examined;
- (ii) Specimens processed by specimen type;
- (iii) Patient cases reported by diagnosis (including the number reported as unsatisfactory for diagnostic interpretation);
- (iv) Gynecologic cases with a diagnosis of HSIL, adenocarcinoma, or other malignant neoplasm for which histology results were available for comparison;
- (v) Gynecologic cases where cytology and histology are discrepant; and
- (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.

(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.

(d) *Workload limits.* The laboratory must establish and follow written policies and procedures that ensure the following:

(1) The technical supervisor establishes a maximum workload limit for each individual who performs primary screening.

(i) The workload limit is based on the individual's performance using evaluations of the following:

(A) Review of 10 percent of the cases interpreted as negative for the conditions defined in paragraph (e)(1) of this section.

(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.

(ii) Each individual's workload limit is reassessed at least every 6 months and adjusted when necessary.

(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—

(i) The maximum number of 100 slides is examined in no less than an 8-hour workday;

(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;

(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

(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.

(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.

(4) Records are available to document the workload limit for each individual.

(e) *Slide examination and reporting.* The laboratory must establish and follow written policies and procedures that ensure the following:

(1) A technical supervisor confirms each gynecologic slide preparation interpreted to exhibit reactive or reparative changes or any of the following epithelial cell abnormalities:

(i) Squamous cell.

(A) Atypical squamous cells of undetermined significance (ASC-US) or cannot exclude HSIL (ASC-H).

(B) LSIL-Human papillomavirus (HPV)/mild dysplasia/cervical intraepithelial neoplasia 1 (CIN 1).

(C) HSIL-moderate and severe dysplasia, carcinoma in situ (CIS)/CIN 2 and CIN 3 or with features suspicious for invasion.

(D) Squamous cell carcinoma.

(ii) Glandular cell.

(A) Atypical cells not otherwise specified (NOS) or specified in comments (endocervical, endometrial, or glandular).

(B) Atypical cells favor neoplastic (endocervical or glandular).

(C) Endocervical adenocarcinoma in situ.

(D) Adenocarcinoma endocervical, adenocarcinoma endometrial, adenocarcinoma extrauterine, and adenocarcinoma NOS.

(iii) Other malignant neoplasms.

(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.

(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.

(4) Unsatisfactory specimens or slide preparations are identified and reported as unsatisfactory.

(5) The report contains narrative descriptive nomenclature for all results.

(6) Corrected reports issued by the laboratory indicate the basis for correction.

(f) *Record and slide retention.* (1) The laboratory must retain all records and slide preparations as specified in §493.1105.

(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.

(3) Documentation of slides loaned or referred for purposes other than proficiency testing must be maintained.

(4) All slides must be retrievable upon request.

(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.

(h) *Documentation.* The laboratory must document all control procedures performed, as specified in this section.

68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§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.

(b) The laboratory must have records that document the following:

(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.

(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.

(3) An adequate number of karyotypes are prepared for each patient.

(c) Determination of sex must be performed by full chromosome analysis.

(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.

(e) The laboratory must document all control procedures performed, as specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 493.1278 Standard:  
Histocompatibility.**

(a) *General.* The laboratory must meet the following requirements:

(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.

(2) All patient specimens must be easily retrievable.

(3) Reagent typing sera inventory prepared in-house must indicate source, bleeding date and identification number, reagent specificity, and volume remaining.

(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.

(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.

(b) *HLA typing.* The laboratory must do the following:

(1) Use a technique(s) that is established to optimally define, as applicable, HLA Class I and II specificities.

(2) HLA type all potential transplant recipients at a level appropriate to support clinical transplant protocol and donor selection.

(3) HLA type cells from organ donors referred to the laboratory.

(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.

(5) Have available and follow written criteria for the following:

(i) The preparation of cells or cellular extracts (for example, solubilized antigens and nucleic acids), as applicable to the HLA typing technique(s) performed.

(ii) Selecting typing reagents, whether prepared in-house or commercially.

(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.

(iv) The assignment of HLA antigens.

(v) When antigen redefinition and re-typing are required.

(6) Check each HLA typing by testing, at a minimum the following:

(i) A positive control material.

(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.

(iii) Positive control materials for specific cell types when applicable

(that is, T cells, B cells, and monocytes).

(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.

(d) *Antibody Screening.* The laboratory must do the following:

(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.

(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.

(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.

(4) Make a reasonable attempt to have available monthly serum specimens for all potential transplant recipients for periodic antibody screening and crossmatch.

(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.

(6) Check each antibody screening by testing, at a minimum the following:

(i) A positive control material containing antibodies of the appropriate isotype for the assay.

(ii) A negative control material.

(7) As applicable, have available and follow written criteria and procedures for antibody identification to the level appropriate to support clinical transplant protocol.

(e) *Crossmatching.* The laboratory must do the following:

(1) Use a technique(s) documented to have increased sensitivity in comparison with the basic complement-dependent microlymphocytotoxicity assay.

(2) Have available and follow written criteria for the following:

(i) Selecting appropriate patient serum samples for crossmatching.

(ii) The preparation of donor cells or cellular extracts (for example, solubilized antigens and nucleic acids), as applicable to the crossmatch technique(s) performed.

(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.

(f) *Transplantation.* Laboratories performing histocompatibility testing for transfusion and transplantation purposes must do the following:

(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—

(i) Testing protocols for cadaver donor, living, living-related, and combined organ and tissue transplants;

(ii) Testing protocols for patients at high risk for allograft rejection; and

(iii) The level of testing required to support clinical transplant protocols (for example, antigen or allele level).

(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.

(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.

(g) *Documentation.* The laboratory must document all control procedures performed, as specified in this section.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

**§ 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.

(b) The laboratory must have a system to identify and assess patient test results that appear inconsistent with the following relevant criteria, when available:

- (1) Patient age.
- (2) Sex.
- (3) Diagnosis or pertinent clinical data.
- (4) Distribution of patient test results.
- (5) Relationship with other test parameters.

(c) The laboratory must document all test result comparison activities.

**§ 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.

(b) The laboratory must document all corrective actions taken, including actions taken when any of the following occur:

(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—

(i) Equipment or methodologies that perform outside of established operating parameters or performance specifications;

(ii) Patient test values that are outside of the laboratory's reportable range of test results for the test system; and

(iii) When the laboratory determines that the reference intervals (normal values) for a test procedure are inappropriate for the laboratory's patient population.

(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.

(3) The criteria for proper storage of reagents and specimens, as specified under § 493.1252(b), are not met.

**§ 493.1283 Standard: Test records.**

(a) The laboratory must maintain an information or record system that includes the following:

(1) The positive identification of the specimen.

(2) The date and time of specimen receipt into the laboratory.

(3) The condition and disposition of specimens that do not meet the laboratory's criteria for specimen acceptability.

(4) The records and dates of all specimen testing, including the identity of the personnel who performed the test(s).

(b) Records of patient testing including, if applicable, instrument printouts, must be retained.

**§ 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.

(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.

(c) The laboratory must document all analytic systems quality assessment activities.

[68 FR 3703, Jan. 24, 2003; 68 FR 50724, Aug. 22, 2003]

## POSTANALYTIC SYSTEMS

**§ 493.1290 Condition: Postanalytic systems.**

Each laboratory that performs non-waived 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.

**§ 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:

(1) Results reported from calculated data.

(2) Results and patient-specific data electronically reported to network or interfaced systems.

(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.

(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.

(c) The test report must indicate the following:

(1) For positive patient identification, either the patient's name and identification number, or a unique patient identifier and identification number.

(2) The name and address of the laboratory location where the test was performed.

(3) The test report date.

(4) The test performed.

(5) Specimen source, when appropriate.

(6) The test result and, if applicable, the units of measurement or interpretation, or both.

(7) Any information regarding the condition and disposition of specimens that do not meet the laboratory's criteria for acceptability.

(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.

(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.

(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.

(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.

(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.

(i) If a laboratory refers patient specimens for testing—

(1) The referring laboratory must not revise results or information directly related to the interpretation of results provided by the testing laboratory;

(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