

testing facility and is therefore responsible for authorizing all testing procedures and any alterations or revisions of these procedures. If a change in directorship occurs, re-approval of the manuals by the new director is necessary since he or she assumes responsibility for all testing procedures and any alterations or revisions of the procedures. We agree with the comment stating that each procedure should be approved by the director before patient testing. Therefore, we are revising the requirement formerly at § 493.1211(d) (now at § 493.1251(d)) to specify that the director reviews each procedure and change in procedure before use. We are also emphasizing that we do not expect laboratories to suspend testing for those procedures already in use that may not have been approved before patient testing. However, effective April 24, 2003, all alterations in current procedures and all newly implemented procedures must be reviewed and signed by the director before use.

In addition, we are revising the requirement formerly at § 493.1211(e) (now at § 493.1251(d)) to include the provision that requires procedures to be re-approved if the directorship changes. Section 493.1251(d) now states, "procedures and changes in procedures must be approved, signed, and dated by the current laboratory director before use." If the directorship changes, the current director would not be expected to suspend testing to review the procedures in use or changes to procedures approved by the previous director. However, the current director must review all procedures in use by the laboratory in a timely manner.

Comment: Approximately one third of the comments received disagreed with § 493.1213, Establishment and verification of method performance specifications. Some individuals opposed verifying the manufacturer's performance specifications for those methods cleared by FDA as meeting certain CLIA requirements for QC. One commenter disagreed with the requirement to establish performance specifications for those methods developed in-house, modified by the laboratory, or not cleared by FDA as meeting certain CLIA QC requirements. Another individual suggested that the standard be retroactive and apply to all test methods. One commenter asked that this standard be revised to state, "The provisions of this section are not retroactive for previously unregulated laboratories. Previously unregulated laboratories are not required * * *."

Response: We understand the commenters' concerns about the time

and resources necessary to establish or verify performance specifications. However, these requirements ensure that the laboratory has either established test system performance specifications or verified that it can obtain the manufacturer's performance specifications in the laboratory's environment using the laboratory's testing personnel. In addition, establishment or verification of performance specifications are integral to the laboratory's establishment of appropriate and effective QC and calibration protocols. These protocols must include descriptions of the numbers, types, and concentrations of all calibration and control materials, as well as the performance intervals. Calibration and control protocols based on unverified performance specifications could result in poorly controlled and inaccurate testing. In the interest of establishing appropriate calibration and control practices and improving the reliability, accuracy, and usefulness of patient testing, we are retaining the requirements formerly at § 493.1213, and are now applying them to nonwaived testing at § 493.1253.

Laboratories employing methods (not modified by the laboratory) that have manufacturer-established performance specifications must demonstrate before reporting patient test results that they can obtain performance specifications for accuracy, precision, and reportable range of test results for the test system, comparable to those established by the manufacturer. The laboratory director must decide the extent to which these performance specifications are verified based on the method, testing conditions, and personnel performing the test.

In addition, we are clarifying when a laboratory must establish test system performance specifications (for example, laboratories using a test system in which the manufacturer does not provide performance specifications) now at § 493.1253(b)(2). Laboratories must, before reporting patient test results, establish, as applicable, performance specifications for the following performance characteristics: (1) Accuracy; (2) precision; (3) analytical sensitivity; (4) analytical specificity, including interfering substances; (5) reportable range of test results for the test system; (6) reference intervals (normal ranges); and (7) any other performance characteristic required for test performance.

Section 493.1253(b)(1) uses the term "FDA-cleared or approved test system" as defined (at § 493.2, Definition) in the November 9, 1997 revisions to the Food, Drug and Cosmetic Act (Pub. L. 105–115), to mean a test system cleared or

approved by the FDA through either the premarket notification (510(k)) or premarket approval (PMA) process for *in-vitro* diagnostic use. This includes test systems exempt from FDA premarket clearance or approval.

Regulations do not have retroactive effect. The CLIA requirement's effective date became applicable to newly regulated laboratories on September 1, 1992. Those laboratories that were subject to regulations prior to this September 1, 1992 effective date were already required to validate test procedures under former Federal regulations before the CLIA requirements were implemented. This rule does not have a retroactive effect. Laboratories performing unmodified moderate complexity tests cleared or approved by the FDA are not required to retroactively verify the manufacturer's performance specifications. The results of the laboratory's control procedures, proficiency testing (required under subpart H) and assessment activities are used to verify test performance. However, as of April 24, 2003, laboratories must, before testing, either verify or establish performance specifications for any new test system.

Comment: Some commenters expressed approval of the requirements for the establishment and verification of a test system's method performance specifications before its use, and maintaining records of this activity while the test system is used for patient testing.

Response: We accept these positive comments and are retaining the requirements for the establishment and verification of method performance specifications formerly at § 493.1213 (now at § 493.1253). However, we realize the QC record retention requirements formerly at § 493.1221 may have been misinterpreted as permitting the laboratory to discard method performance specification records after a 2-year period even though the method may have continued to be used beyond this timeframe. Therefore, the analytic systems record retention requirement formerly at § 493.1221 (now at § 493.1105(a)(3)(i)) specifies that records of the laboratory's establishment and verification of method performance specifications must be retained for the period of time the test system is in use by the laboratory, but not less than 2 years. In addition, we are revising the original QC record retention requirement to accommodate the reorganization of the regulation and clarify its intent.

Comment: A few commenters disagreed in general with the