

subtle changes in test system performance, environmental conditions, and variance in operator performance (for example, different operators and same operator variations in specimen handling and testing).

In response to the comments concerning unit use test systems and the use of procedural controls, we are making allowances for the use of procedural controls in Appendix C of the State Operations Manual (CMS Pub. 7) when equivalent quality procedures can be demonstrated.

In addition, we are providing a definition for test system (now at § 493.2). A test system is the instructions and all of the instrumentation, equipment, reagents, and/or supplies needed to perform an assay or examination and generate test results.

A control material must detect errors in the entire testing process. It must also monitor the quality of the results provided by the test system. It may be supplied by the test system manufacturer or another source. We are also relocating the requirement for control materials to be tested in the same manner as patient samples formerly at § 493.1218(c) (now at § 493.1256(d)(8)) and clarifying that this requirement applies to control materials and that over time control testing must be rotated among all operators who perform the testing (now at § 493.1256(d)(7)).

We are reducing the frequency of testing control materials from "each run" to "each day of testing." We are retaining the former requirements for qualitative procedures (test positive and negative control materials) and quantitative procedures (test two levels of control material). For test procedures producing graded or titered results, we are relocating the requirement to test a negative control and a control of graded or titered reactivity from Syphilis serology and General immunology formerly at §§ 493.1239(b) and 493.1241(a), respectively (now at § 493.1256(d)(3)(iii)).

As part of updating the requirements for new technology and test methodologies formerly at § 493.1218(b)(3) (now § 493.1256(d)(5)), we are revising the wording of the control requirement for electrophoresis procedures.

*Comment:* One commenter urged that we remove specific stipulations for frequencies of performing QC or calibrations and substitute reference to an agency or professional association guidelines. The commenter also recommended that we accept alternate approaches suggested by a manufacturer

as documented in test system instructions approved by the FDA. Another commenter suggested that § 493.1218(a) be revised to state, "that the laboratory should run controls as specified by the manufacturer's instructions." Several commenters and one organization stated it is the laboratory director's responsibility to design the control system needed to achieve the desired quality.

*Response:* We consider the requirements established in subpart K as the minimum control measures needed to ensure accurate and reliable test results. According to the requirements formerly at § 493.1213 (now at § 493.1253), each laboratory must verify or establish a test system's method performance specifications and use this information in determining appropriate calibration and control protocols. This may include more frequent testing and greater numbers of materials than specifically provided under CLIA regulations. For example, the laboratory is required to perform calibration and control procedures in the manner necessary to ensure quality results. In cases where the manufacturer's instructions require more stringent testing of calibrators, control materials, or both, the laboratory is required to follow the manufacturer's instructions. Therefore, we are clarifying that laboratories must follow the manufacturer's instructions for control testing if they meet or exceed the requirements now at § 493.1256(d)(3).

We agree with the comment concerning the laboratory director's responsibility to determine appropriate control procedures to monitor the complete analytical process. This requirement is specified in CLIA regulations under the director's responsibilities at § 493.1407(e)(5) for moderate complexity testing and § 493.1445(e)(5) for high complexity testing.

*Comment:* A commenter suggested that acceptable control materials are two samples of different concentrations of controls or two concentrations of calibration material of a different lot other than the lot used for assay calibration, or any combination that results in both normal and abnormal values.

*Response:* We agree with the commenter and emphasize that any calibrator used as control material must be of a different lot number than the one(s) used to establish a cutoff value or calibrate the assay. Therefore, we are revising this requirement formerly at § 493.1218(b)(2) (now at § 493.1256(d)(9)) to clarify that the calibrators used as control materials

must be of different concentrations than the calibrators employed to set instrumentation. We recommend that the acceptable range of control materials reflect some clinical decision points, both normal and abnormal.

*Comment:* One commenter suggested that § 493.1218(d) be revised to include a provision that if the performance specifications at § 493.1213 are exceeded, the laboratory must take corrective action before patient testing can continue.

*Response:* We agree with the commenter. The requirements formerly at § 493.1219(a) (now at § 493.1282(b)(1)) require corrective action, and the requirements formerly at § 493.1701 (now at § 493.1289(b)) require the laboratory to review the effectiveness of its corrective actions and, if necessary, revise policies and procedures to prevent recurring problems.

*Comment:* One commenter disagreed with the requirement to check each batch or shipment of media.

*Response:* The CLIA regulations allow laboratories to use the manufacturer's QC checks of certain media, provided the manufacturer's product insert specifies that the manufacturer's QC checks meet the NCCLS standards for media QC formerly at § 493.1218(f)(4), now addressed in Appendix C of the State Operations Manual (CMS Pub. 7). For media not included by NCCLS, we believe it is critical that the laboratory check each batch of media to ensure that it is not contaminated, supports growth of appropriate organisms, and elicits the correct biochemical response(s). The former § 493.1218(f)(4) (now § 493.1256(e)(4)) clarifies that media checks must be performed before, or concurrent with, initial use of media.

*Comment:* A few commenters expressed disagreement with the requirement to evaluate the detection phase of direct antigen systems and the extraction phase when it is included.

*Response:* We believe the laboratory must verify that all steps of a testing procedure are functioning properly to prevent erroneous results. Therefore, we are retaining the requirement formerly at § 493.1218(b)(4) (now at § 493.1256(d)(3)(iv)) that requires laboratories to test two control materials, one that is capable of detecting errors in the extraction phase.

*Comment:* One commenter agreed with requiring the determination of statistical parameters for each lot of calibration or control materials.

*Response:* We are retaining the requirement formerly at § 493.1218(d)(2) (now at § 493.1256(d)(10)(i)) for laboratories to have statistical